

RADIOLOGY

A MONTHLY JOURNAL DEVOTED TO CLINICAL RADIOLOGY AND ALLIED SCIENCES

Vol. 61

DECEMBER, 1953

No. 6

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RADIOLOGY

A MONTHLY PUBLICATION DEVOTED TO CLINICAL RADIOLOGY AND ALLIED SCIENCES
PUBLISHED BY THE RADIOLOGICAL SOCIETY OF NORTH AMERICA

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Henry Ford Hospital, Detroit 2, Mich.

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Endocardial Fibroelastosis

With a Case Presentation¹

MARVIN N. GOLPER, M.D.²

THIS PAPER deals with an entity which has been referred to as endocardial sclerosis, fetal endocarditis, and endocardial fibroelastosis. Although it has received considerable attention in recent pediatric and pathologic literature, it has not been discussed in radiologic literature, despite the fact that radiologists will see these cases and may be in a position to suggest the diagnosis. It is of particular importance in this day of corrective cardiovascular surgery, for it is among the cardiac conditions which may produce cyanosis but cannot be surgically corrected by present methods.

PATHOGENESIS

In endocardial fibroelastosis there is cardiac enlargement due both to hypertrophy of the myocardium of the left ventricle and dilatation as a result of failure. The endocardium of the left ventricle is thickened and fibrotic; rarely, similar changes are present on the right. The endocardium has a thick, white, opaque appearance which usually involves the entire lining of the ventricle and may extend into the left atrium. Valvular changes, consisting of contractures, thickening of the valve leaflets, and occasional adhesions of the leaflets can sometimes be seen. Microscopically, the endocardium reveals fibrous and

elastic tissue thickening without evidence of inflammation. Changes in other organs are secondary to chronic congestion and failure.

It is believed that the endocardial fibrosis interferes with the normal emptying of the arterioluminal vessels into the ventricular cavity, the elastic tissue producing constriction of their orifices. Weinberg and Himelfarb (11) postulate that the resultant partial stasis of the blood stream produces anoxemia, dilatation, and ventricular failure. Myocardial hypertrophy results only if the patient lives long enough.

The earliest description of the gross pathological changes is said to have been made in 1818 by Kreysig. Several others reported similar cases in the early nineteenth century and suggested intra-uterine inflammation as the most likely etiologic factor, and this explanation was widely accepted at the end of that century. There was difference of opinion as to whether the agent was toxic or bacterial. As more observers studied the microscopic changes, reports began to favor a congenital or developmental defect as the cause. Though controversy persists, most recent observers favor the latter view. Prior and Wyatt (8) could find no evidence of inflammation in the mural and valvular lesions and regard this condition as a

¹ Accepted for publication in January 1953.

² Director of Radiology, St. Joseph Memorial Hospital, Kokomo, Ind.

developmental disorder of the mesenchymal tissue, to be classified with congenital cardiac malformations. More recently, Hill and Reilly (6) have presented evidence based on tissue staining which suggests that this may be one of the collagen diseases, but Adams and Katz (1) disagree with this view, giving as reasons the rare involvement of the myocardium, lack of microscopic evidence of inflammation within the myocardium, failure of acute phase protein elevation, and the occasional presence of elastic fibers in the heart valves of these patients.

On the basis of evidence, the inflammation theory seems unlikely. As pointed out by Sano and Anderson (9), there is a marked hyperplasia of elastic tissue in the thickened endocardium, and Weinberg and Himelfarb suggested that the condition be called "endocardial fibroelastosis." The present writer believes this to be the term of choice.

CLINICAL FINDINGS

Observers are agreed that endocardial fibroelastosis occurs primarily in infancy and childhood. In a majority of cases death has occurred before the age of six months. Although "sudden death" may result, more often there are premonitory symptoms of short duration. Some of these patients, as Lewis (7) has recently shown, may respond to oxygen and digitalis and may be maintained on digitalis for a relatively long period. Major symptoms include dyspnea, listlessness, vomiting, and occasionally cyanosis.

The physical findings consist usually of dyspnea, râles in the lungs, marked cardiac enlargement with distant heart tones of poor quality, and possibly liver enlargement. Peripheral edema may be present. Since the heart failure may be precipitated or accompanied by a respiratory infection, the patient may be acutely ill and febrile. Presence of a murmur in either the mitral or aortic region will depend on the degree of pathologic involvement of these valves.

Blood findings, urinalysis, and sedimentation rate are usually normal unless a

secondary infection is present. The electrocardiogram may reveal a normal or left axis deviation, but Adams and Katz point out that unipolar precordial leads usually reveal evidence of marked left ventricular hypertrophy. There are also low, negative, or diphasic T waves, changes compatible with heart strain and anoxemia.

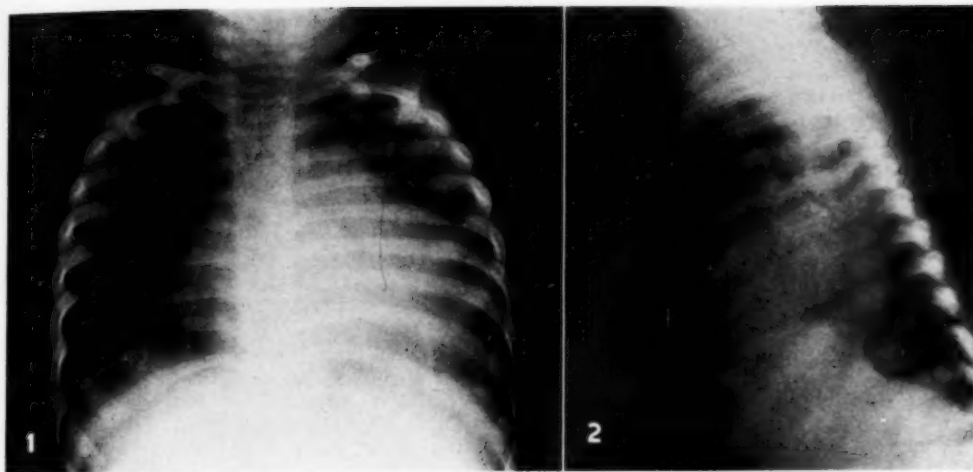
ROENTGEN FINDINGS

The radiographic and fluoroscopic findings will depend on the degree of cardiac involvement and the presence or absence of heart failure.

Enlargement of the left ventricle is first manifested in the anteroposterior view by elongation and greater convexity on the left, projecting the cardiac apex farther caudad. With greater enlargement there will be an actual increase in the size of the heart to the left and posteriorly, the latter best seen in the left oblique position. In the lateral position, encroachment upon the retrocardiac space is visualized. With gross enlargement of the left ventricle, there will be widening to the right as well as to the left and posterior, by actual displacement of the right chambers toward that side.

Enlargement of the left atrium will occur in the cases in which mitral valvular involvement has produced a stenosis. It is best recognized in an early stage in the right oblique position, as it will cause a posterior compression displacement of the barium-filled esophagus. With marked enlargement of this chamber, its density is increased and may be recognized within the cardiac shadow. It may eventually extend to the right of the right upper cardiac border, producing the so-called "double right upper cardiac border." The latter is seen in the anteroposterior view.

If the patient is seen during failure, the cardiac silhouette tends to assume a triangular shape, due to the marked enlargement in all directions. The left ventricular enlargement, however, is usually out of proportion to the dilatation of the other chambers. This results in a globular distortion of the triangle with a slight per-



Figs. 1 and 2. Anteroposterior and lateral views of the chest showing a markedly enlarged heart of globular shape but with definite prominence of the left ventricle. Slight pulmonary congestive changes are present. The pulmonary artery is not prominent.

sistence of the rounded character on the left side. The lung changes consist of vascular engorgement at the hili as well as increased vascular shadows in the inner zones and bases. With progression, there is a mottled irregular increase in density of the lung fields, diminishing peripherally from the hili.

PROGNOSIS

Some patients succumb before the clinical diagnosis is suspected. Others may have recurrent attacks of left heart failure usually precipitated by a respiratory infection. Some respond to oxygen and digitalis.

DIFFERENTIAL DIAGNOSIS

The differential diagnosis is best discussed on the basis of the presence or absence of cardiac murmurs. In their absence myocarditis must be considered, but the predominantly left-sided rather than generalized enlargement will help eliminate that condition. Moreover, the usual prolonged conduction and lowered voltage of the various complexes in myocarditis are not seen in the electrocardiogram. In the presence of murmurs, differentiation must be made from the more common congenital cardiac malformations.

Roentgenologically the absence of increased pulmonary vascularity and prominent pulmonary artery will help rule out lesions with a left-to-right shunt. Right axis deviation will be absent. Patients with a congenital mitral or aortic lesion usually have a benign course early in infancy and their electrocardiographic changes show no evidence of the anoxemia seen in those with endocardial fibroelastosis.

CASE PRESENTATION

D. K., a white male of twenty-one months, was admitted to the St. Joseph Memorial Hospital on Oct. 3, 1951. He was the second child of normal healthy parents and his birth at term had been uneventful. His parents thought his postnatal progress normal but felt that he was somewhat apathetic.

He had been seen by the family physician five days previously because of a febrile respiratory infection. Penicillin was given intramuscularly. On the third day prior to admission, edema of the lower eyelids and a moderate edema of the lower extremities developed. Admission to the hospital was by a pediatric consultant.

Additional physical findings on admission included moderate distention of the neck veins and slight edema of the entire face. The child appeared lethargic and pallid, but no cyanosis was believed to be present. The breath sounds were tubular, and occasionally moist and dry râles were heard posteriorly at the left base. The heart was markedly enlarged to the left, with the apex beat palpable in the left mid-axillary line. The cardiac rate was rapid

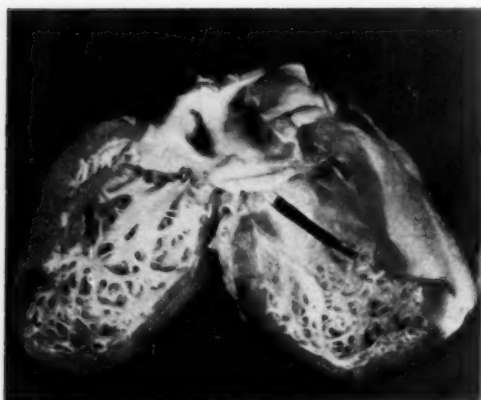


Fig. 3. Opened heart, showing the opaque, white, thickened endocardium of the left ventricle.

but regular. No murmurs were heard, but the heart tones were faint. No thrill was palpable. The liver was slightly enlarged. The blood pressure was 100/70. Rectal temperature was normal. The pulse was recorded as "rapid."

Laboratory examination of the blood revealed a hemoglobin of 9.8 grams (68 per cent), with 4,020,000 red cells and 14,300 white cells (35 per cent neutrophils with one band, 60 per cent lymphocytes, and 5 per cent monocytes). The red blood cells disclosed anisocytosis and poikilocytosis. The platelets were normal. Urinalysis was normal, but the specific gravity of a single specimen was 1.002. Total proteins were 4.0 grams, with 2.5 grams of albumin and 1.5 grams of globulin.

On the evening of the second day following admission the patient became more dyspneic, and moderate cyanosis was present. A consultant cardiologist found no additional physical signs, and an electrocardiogram obtained on the following morning was interpreted as showing "sinus tachycardia, left axis deviation, and a non-specific abnormality of QRS complexes and T waves."

Radiographic and fluoroscopic examination of the chest revealed gross enlargement of the heart, predominantly left-sided, although chamber differentiation was difficult because of feeble pulsations. Slight pulmonary congestion was believed to be present (Figs. 1 and 2).

The clinical impression at this time was myocarditis with probable effusion and failure. Oxygen was administered, and chloromycetin was given for probable pneumonitis. ACTH was started at noon on the third day. The pediatrician visited the patient at 5:15 P.M. and noted nothing new. Fifteen minutes later a nurse noted that the child was sleeping restlessly. At 6:00 P.M. the same nurse found him dead.

An autopsy was performed by Dr. Max W. Rudicel, pathologist. The necropsy report was as follows:

"The body was 33 in. in length and estimated to weigh 25 to 30 pounds. There was a grade one edema of the eyelids, scrotum, and ankles, with similar mild edema throughout the soft tissues internally. The transverse pericardium measured 12 cm., and the apex was 1 cm. from the left lateral chest wall. The heart weighed 135 grams compared to 60 grams normal for a child of this size; it completely filled the pericardial sac, and the pericardial surfaces were smooth, with no excess fluid present. The contour was globular, due to dilatation of all chambers. No lesions were observed on the endocardium or valves on the right. The aortic valve appeared normal. The entire endocardial surface of the left atrium and left ventricle was covered by a white, opaque layer of tissue almost 1.0 mm. in thickness (Fig. 3). The mitral valve was slightly thickened but pliable and capable of competent function. This thickened endocardium was microscopically seen to be composed of fibrous and elastic tissue, the latter component being well demonstrated by Verhoeff's stain (Fig. 4). The heart measurements, including valves, were: aortic, 3.5 cm.; mitral, 6.3 cm.; tricuspid, 6.5 cm.; pulmonary, 3.7 cm.; thickness of right ventricle, 2.0 to 3.0 mm.; thickness of left ventricle, 9 mm. No congenital defects of the septa were observed. The foramen ovale was closed and the ductus arteriosus was obliterated. Sections of the myocardium showed no involvement in the process, with cross-striations preserved and no evidence of degeneration or inflammatory infiltration. A few small arteries beneath the endocardium showed swelling of endothelial cell linings, with some pale blue vacuoles in an immediate subendothelial position.

"Scattered dark blue areas of focal atelectasis were present in the lungs, with a fairly large confluent area on the left, where the enlarged heart had exerted its pressure. In sections, an early developing suppurative pneumonitis was found in the right lower lobe. There were no 'heart failure' cells. No other evidence of chronic passive congestion was observed. Changes in the remaining organs were those of acute congestion, most prominent in the liver.

Permission was not granted for central nervous system examination, but a specimen of cisternal cerebrospinal fluid was sparkling clear, with a protein content of 22 mg. per cent and a non-protein nitrogen of 55 mg. per cent.

"Final anatomical diagnoses: endocardial fibroelastosis, left chambers and mitral valve of heart; cardiac hypertrophy, 135 grams; cardiac dilatation."

CONCLUSIONS

If endocardial fibroelastosis is kept in mind, it is felt that the condition may be diagnosed antemortem. Given an infant or young child (1) in an episode of left

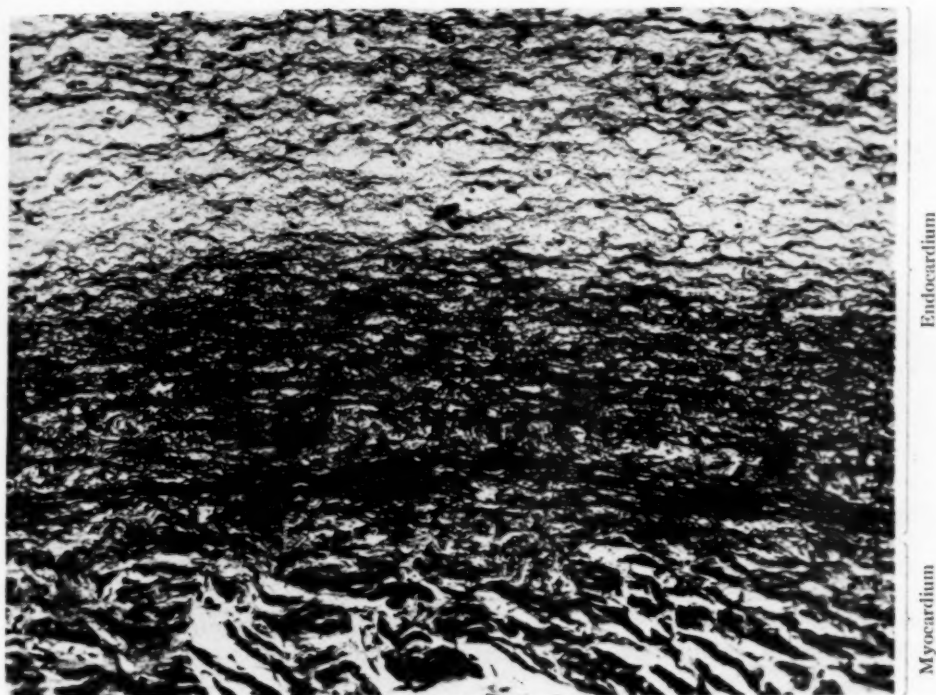


Fig. 4. Photomicrograph of a section through the left ventricle revealing the thickened endocardium. Elastic tissue appears black and fibrous tissue white (Verhoeff's stain).

heart failure, usually following an upper respiratory infection, (2) with electrocardiographic evidence of marked left ventricular hypertrophy and anoxemia, and (3) with roentgen findings of gross cardiac enlargement, predominantly left ventricular, a presumptive clinical diagnosis may be made.

SUMMARY

The gross and microscopic cardiac findings in endocardial fibroelastosis and the etiologic theories have been discussed.

The typical signs, symptoms, physical and laboratory findings, and roentgen features have been described, and a typical case has been presented.

It is concluded that endocardial fibroelastosis may be diagnosed clinically.

NOTE: The author is indebted to Reuben Craig, M.D., for permission to report the case presented and to J. F. Glone of the Medical Illustration Department of the Indiana Medical Center for the photographic reproductions.

ADDENDUM: Recently, an apparently normal male infant of three days died suddenly in our hospital after a short episode of cyanosis and labored rapid breathing. No roentgen studies were done. Postmortem findings were almost identical with those in the case presented—another example of endocardial fibroelastosis.

1907 W. Sycamore Rd.
Kokomo, Ind.

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SUMARIO

Fibroelastosis Endocardiaca, con Una Observación

Histopatológicamente, caracterízase la fibroelastosis endocardiaca, también denominada esclerosis endocardiaca y endocarditis fetal, por aumento del volumen del corazón debido tanto a hipertrofia del miocardio del ventrículo izquierdo como a dilatación consecutiva a la insuficiencia. Al microscopio, el endocardio revela espesamiento del tejido fibroso y elástico sin signos de inflamación. El estado pasa hoy día generalmente por ser debido a un vicio congénito o del desarrollo.

La fibroelastosis endocardiaca es una enfermedad de la infancia y la niñez, terminando habitualmente en la muerte antes

de la edad de seis meses. Los síntomas principales son disnea, apatía, vómitos y, en ocasiones, cianosis. Puede haber edema periférico. Cabe sospechar el diagnóstico clínicamente en un lactante o niño pequeño observado en un episodio de insuficiencia del corazón izquierdo a continuación de una infección de las vías aéreas superiores, con signos electrocardiográficos de pronunciada hipertrofia del ventrículo izquierdo y anoxemia, y con signos roentgenológicos de hipertrofia macroscópica del corazón, con predominio en el ventrículo izquierdo.

Preséntase un caso típico, con los hallazgos autopsicos.



Differential Diagnosis of Right Cardiophrenic Angle Masses¹

JAMES V. ROGERS, JR., M.D., and TED F. LEIGH, M.D.

THE RIGHT cardiophrenic angle is not an uncommon site for tumefactive lesions. Many of these are asymptomatic. Fortunately, most are benign, but occasionally a mass in this location is malignant. It is important, therefore, to make a definitive diagnosis when possible.

Since most masses in the cardiophrenic angle are unsuspected clinically and are found only on roentgenographic examination of the chest, it behooves the radiologist to be familiar with the lesions that may occur in this location. His decision will many times serve to guide the clinician in the proper handling of the patient.

In the last several years, we have had the opportunity of studying 16 patients with right cardiophrenic angle masses, the nature of which was established either by roentgenologic procedures or by operation. We have seen an equal number of cases in which the diagnosis was not proved. At the present time, we feel some confidence in the accuracy of a preoperative diagnosis based on the roentgenologic findings.

In the roentgen study of these masses, we have found the following procedures useful. Rarely, however, do we find it necessary to perform all of them in an individual case.

- (1) Routine postero-anterior and right lateral chest films for identification of the lesion.
- (2) Fluoroscopy to determine the position of the mass in relation to adjacent structures, variations in size and shape with respiration, and the presence of transmitted or intrinsic pulsations.
- (3) Tomograms of the right cardiophrenic angle in frontal and lateral projections for better delineation

of the mass and its relation to adjacent structures.

- (4) An abdominal film or barium enema study for localization of the transverse colon.
- (5) Upright chest films following pneumoperitoneum.
- (6) Upright and decubitus films following pneumothorax.
- (7) Occasionally an angiocardigram or bronchogram.

For the purposes of description and simplicity, we classify right cardiophrenic angle masses as follows: (A) congenital pericardial celomic cysts and diverticula; (B) omental herniations through the right foramen of Morgagni; (C) all other masses arising from the structures bordering the right cardiophrenic angle.

Of our 16 proved cases, 6 were in class A, 6 in Class B, and 4 in Class C.

A. CONGENITAL PERICARDIAL CELOMIC CYSTS AND DIVERTICULA

Lambert (14) described congenital pericardial celomic cysts and diverticula in detail in 1940, and since that time nearly a hundred cases have appeared in the literature (1-4, 13, 15-18, 22). According to Lambert, the pericardium is formed by the fusion of several mesenchymal lacunae. Failure of fusion of one or more of these results in the formation of a congenital pericardial celomic cyst, and an incomplete fusion results in a pericardial diverticulum, which communicates with the pericardium. Celomic cysts and diverticula may occur in any location adjacent to the pericardium but the majority are in the right cardiophrenic angle; all of them are within the mediastinum. They vary from a few centimeters in diameter to considerable size. The smaller ones are quite pliable

¹ From the Department of Radiology, Emory University School of Medicine, Atlanta, Ga., and Emory University Hospital, Emory University, Ga. Read by title and presented as an exhibit at the Thirty-eighth Annual Meeting of the Radiological Society of North America, Cincinnati, Ohio, Dec. 7-12, 1952.

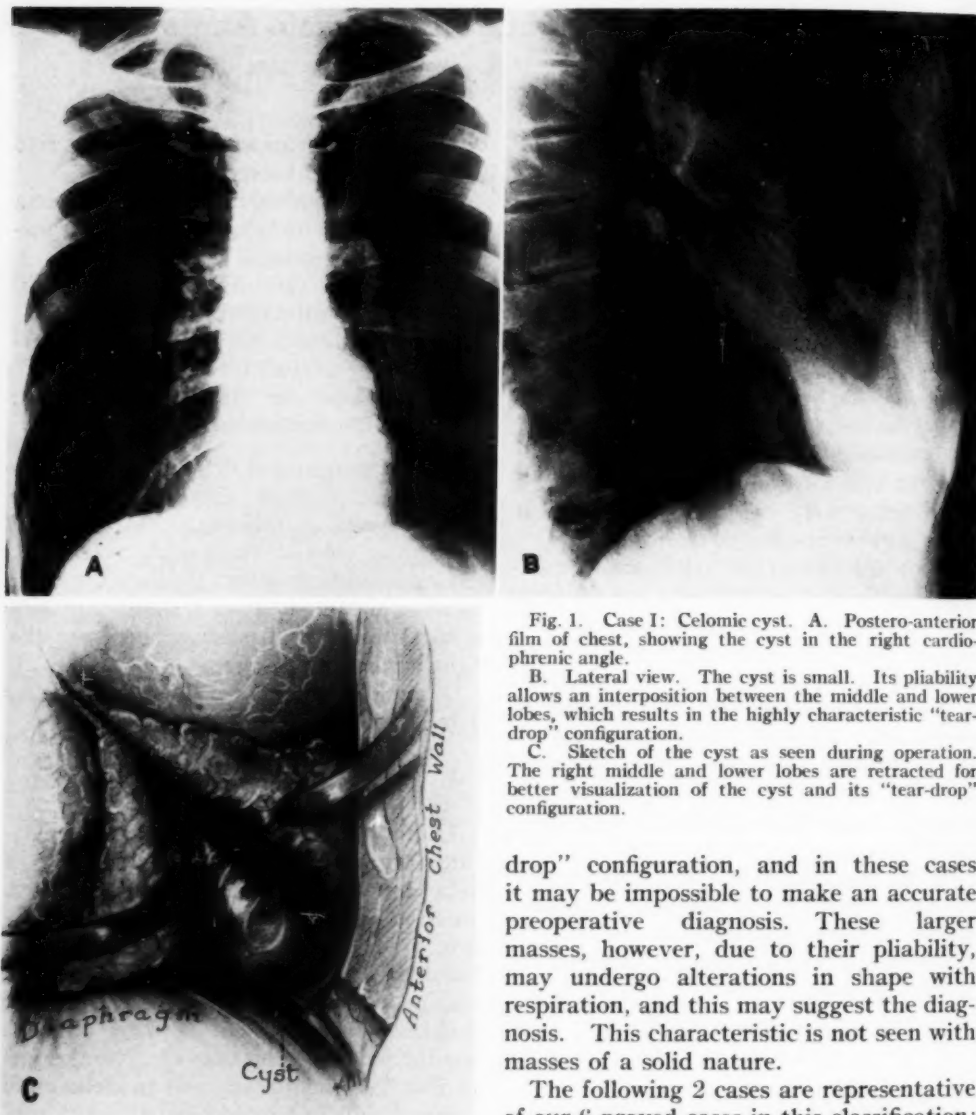


Fig. 1. Case I: Celomic cyst. A. Postero-anterior film of chest, showing the cyst in the right cardiophrenic angle.

B. Lateral view. The cyst is small. Its pliability allows an interposition between the middle and lower lobes, which results in the highly characteristic "tear-drop" configuration.

C. Sketch of the cyst as seen during operation. The right middle and lower lobes are retracted for better visualization of the cyst and its "tear-drop" configuration.

drop" configuration, and in these cases it may be impossible to make an accurate preoperative diagnosis. These larger masses, however, due to their pliability, may undergo alterations in shape with respiration, and this may suggest the diagnosis. This characteristic is not seen with masses of a solid nature.

The following 2 cases are representative of our 6 proved cases in this classification:

CASE I: F. M. J., a 57-year-old practicing physician, was in excellent health. In December 1950, a routine chest examination disclosed the presence of a mass in the right cardiophrenic angle. This appeared rounded in the frontal view, but a lateral film showed a "tear-drop" configuration (Fig. 1A and B). At operation, a lemon-sized cyst was found and easily removed (Fig. 1C). The final diagnosis was pericardial celomic cyst.

CASE II: J. T. C., a 37-year-old asymptomatic white male, was admitted to Emory University Hospital in September 1947, for investigation of a

(due to their thin walls and fluid content) and, because of this, they project into the fissure between the middle and lower lobes, assuming a "tear-drop" configuration when viewed on the lateral film. This "tear-drop" shape is highly characteristic (Fig. 1B and C).

Since the larger cysts or diverticula are not interposed between the middle and lower lobes, they do not have a "tear-

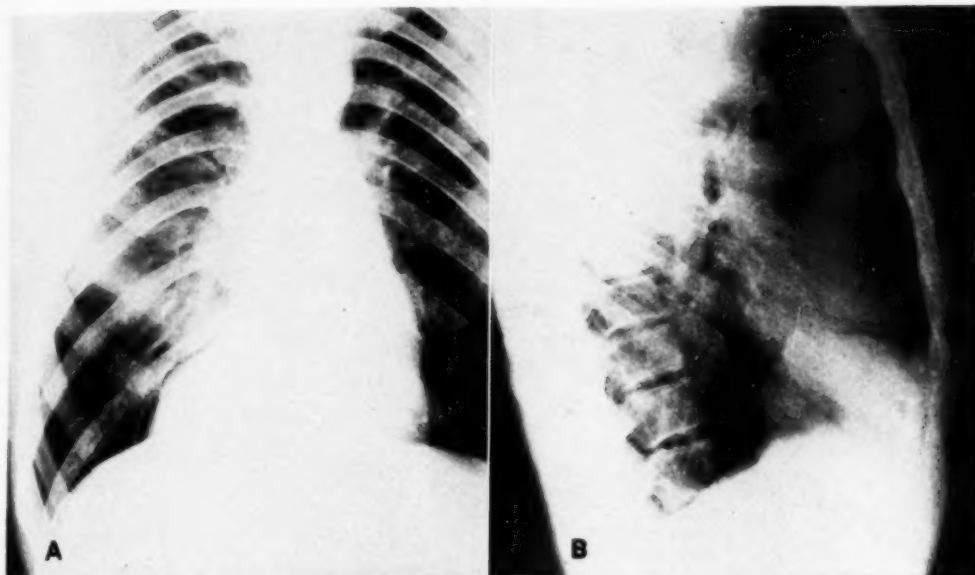


Fig. 2. Case II: Celomic cyst. A. Frontal view, showing a relatively large cyst in the right cardiophrenic angle.

B. Lateral view. There is slight "tenting" of the cyst into the interlobar fissure superiorly. Usually the larger cysts do not show this sign.

right cardiophrenic angle mass (Fig. 2A and B). Fluoroscopically this could be separated from the anterior chest wall, but not from the diaphragm and mediastinum. At operation the mass was found to contain fluid; it was attached to the pericardium by a pedicle, but did not communicate with the pericardial sac. The cyst and pedicle were removed without difficulty. The final diagnosis was pericardial celomic cyst.

B. OMENTAL HERNIATIONS THROUGH THE RIGHT FORAMEN OF MORGAGNI

The foramen of Morgagni is a congenital deficiency in the musculature of the diaphragm at either side of its sternal attachment, resulting in two small triangular apertures whose bases are located anteriorly. These openings, covered above by pleura and below by peritoneum, contain loose areolar tissue. Lymphatics and the superior epigastric arteries course through them (9, 27).

Omental herniations through this portion of the diaphragm may be congenital or acquired, and usually are covered by a peritoneal sac. In the younger age groups, the intestine frequently herniates through these openings, whereas in the older age

groups it is omentum that herniates. Women are especially prone to omental herniations, accounting for 5 of our 6 cases. Increased intra-abdominal pressure, as in pregnancy, appears to be an important factor. The attachment of the pericardium to the diaphragm affords good protection to the foramen on the left, and for that reason herniations are less common there than on the right.

Roentgenologically, omental herniations are identified by the following features (23, 25): (a) They cannot be separated from the diaphragm. (b) They may become smaller with expiration (because of partial reduction of the hernia with decreased intra-abdominal pressure). (c) The transverse colon is frequently elevated and presents an inverted V or U shape. (d) Following pneumoperitoneum, air usually enters the sac and can be identified on roentgenograms.

The following case is representative of the 6 in this classification.

CASE III: Mrs. J. W. M., a 71-year-old white woman, gave a history of chronic cough, occasionally

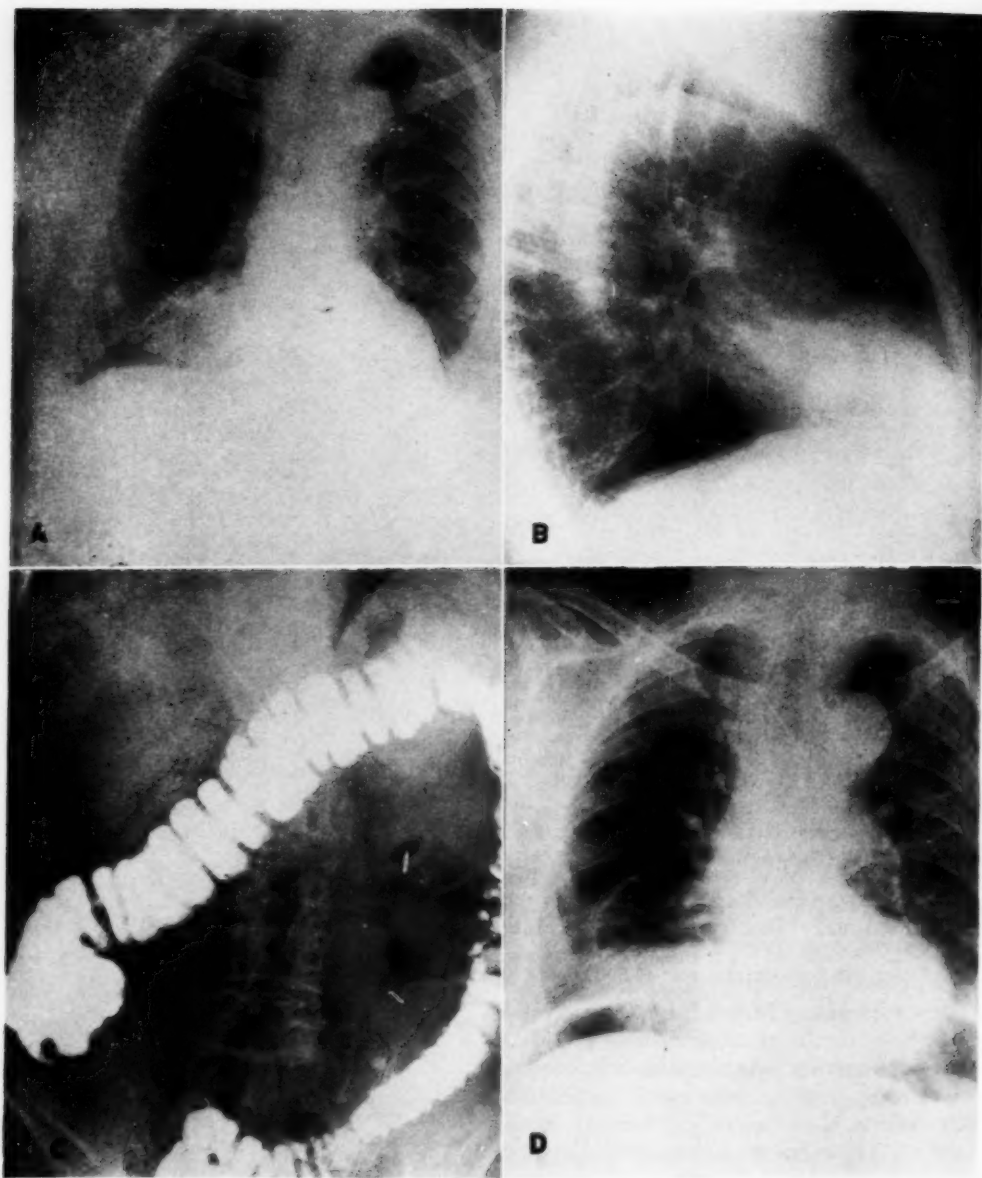


Fig. 3. Case III. Omental herniation through the right foramen of Morgagni. A. Routine frontal view, showing the mass in the right cardiophrenic angle.

B. Right lateral view of the herniated omentum, showing its anterior location.

C. Barium enema study. The transverse colon is slightly elevated. Characteristically, the elevation is more pronounced and simulates an inverted "V" or "U."

D. Postero-anterior chest film following pneumoperitoneum. Some of the instilled air is present in the sac. There is no significant change in the volume of the mass. Not infrequently a partial or complete reduction of the hernia will occur with this procedure.

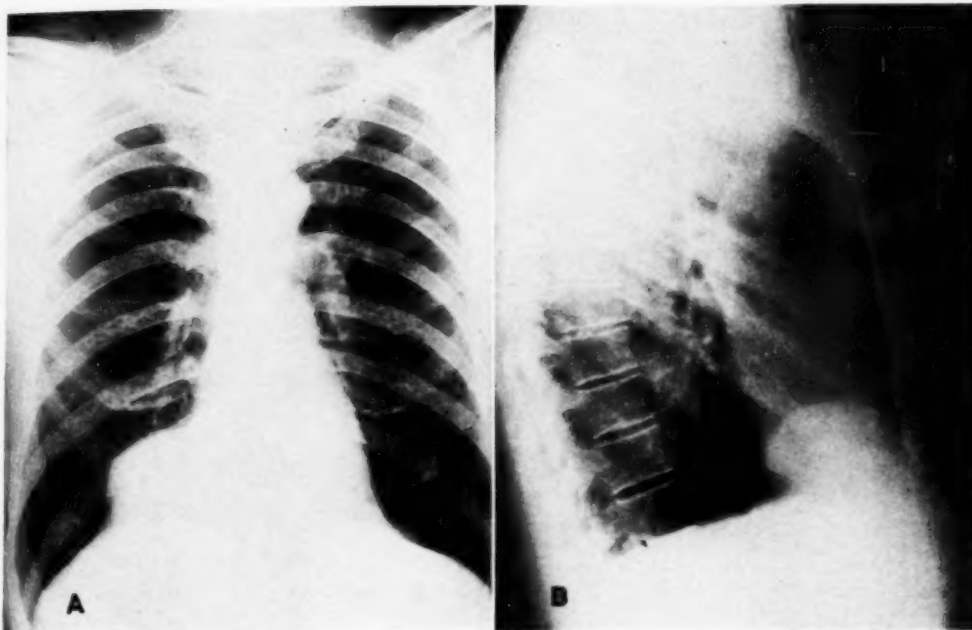


Fig. 4. Case IV: Anterior mediastinal cyst, unclassified. A. Frontal view, showing a relatively large mass in the right cardiophrenic angle.

B. Lateral view. The base of the mass is against the diaphragm. Note its resemblance in size and position to an omental herniation or a celomic cyst.

productive of thick white sputum. She infrequently experienced mild chest pain, which she attributed to a steering wheel injury sustained in an automobile accident fifteen years earlier. In May 1952, chest roentgenograms had disclosed a moderately large mass in the right cardiophrenic angle (Fig. 3A and B). Further investigation of this lesion by barium enema examination showed a mild upward displacement of the transverse colon (Fig. 3C). Chest films following pneumoperitoneum definitely established the nature of the lesion (Fig. 3D). Surgical intervention was not thought to be indicated. The final diagnosis was right foramen of Morgagni herniation with omentum in the hernial sac.

C. ALL OTHERS

This group, as stated previously, includes all lesions that may occur in the right cardiophrenic angle other than the congenital pericardial cysts and diverticula and omental herniations through the right foramen of Morgagni. Rarely is it possible to make a specific diagnosis in this group without surgery. The roentgen investigation, therefore, is directed toward

determining the site of origin (mediastinum, lung, chest wall, etc.) (7, 12, 19, 21, 24, 26).

Right-sided pericardial fat pads (11), pleural reflections over the inferior vena cava, pleural thickenings, and segmental eventrations of the diaphragm sometimes resemble a mass in the frontal view, but when studied in the lateral projection should be identifiable.

A localized collection of fluid in the pleura, pericardium (inflammatory diverticulum) (6), or mediastinum may at times enter into the differential diagnosis of right cardiophrenic angle lesions.

Our 4 cases in this group included a carcinoma of the thymus, a lipoma arising in the thymus, an anterior mediastinal cyst (unclassified), and a traumatic rupture of the right diaphragm, with herniation of a portion of liver. Two of these cases are presented.

CASE IV: J. C. was a 57-year-old white male. Routine roentgenograms revealed a rounded mass in

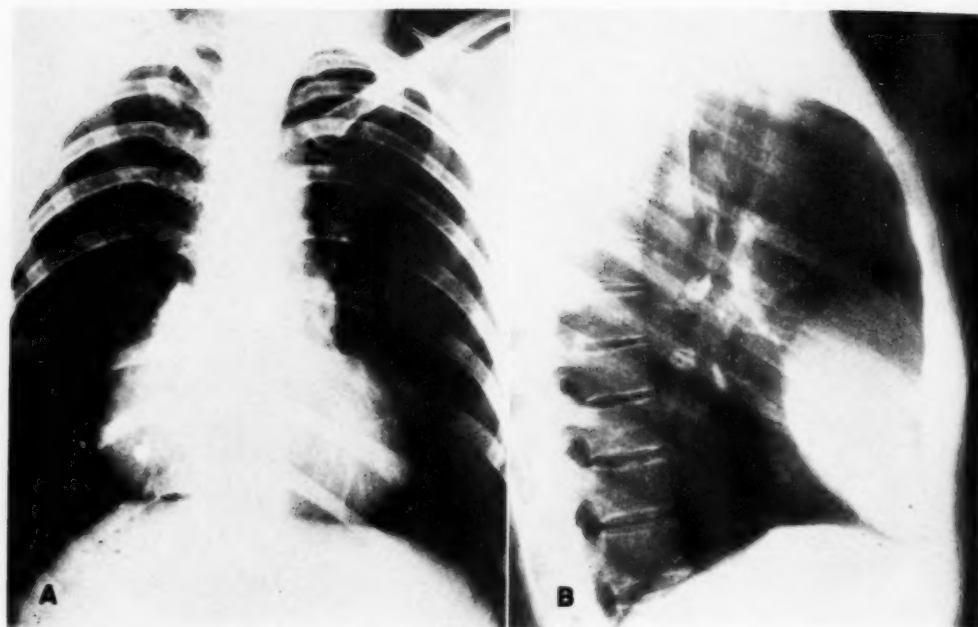


Fig. 5. Case V: Carcinoma of the thymus. A. Frontal view, showing the large mass in the right lower mediastinum.

B. Lateral view, showing the anterior position of the tumor. The inferior border of the mass is above the diaphragm.

the right cardiophrenic angle, which could not be separated fluoroscopically from the diaphragm or mediastinum (Fig. 4A and B). There were no symptoms. No air entered the mass following pneumoperitoneum. The mass was surgically removed and proved to be a multiloculated cyst containing necrotic material and large amounts of cholesterol. No specific diagnosis could be made. The final diagnosis was anterior mediastinal cyst, unclassified.

CASE V: Mrs. M. S. C., a 40-year-old chronically ill white woman, was admitted for a panhysterectomy. Chest roentgenograms showed a large mass in the right cardiophrenic angle (Fig. 5A and B). In 1944, bone marrow studies made because of a persistent low white count led to a diagnosis of aleukemic leukemia. On the present admission, the white count was 4,650, with 21 segmented forms, 12 band forms, 40 lymphocytes, and 27 monocytes. Because of the leukopenia, panhysterectomy was deferred. The patient went steadily downhill, and died approximately one month following admission. Postmortem examination revealed a solid tumor, weighing 260 grams, in the right lower anterior mediastinum. The final pathologic diagnosis was carcinoma of the thymus.

CONCLUSIONS

From our study of these 16 proved cases,

we have reached certain definite conclusions:

The diagnosis of many right cardiophrenic angle masses can be established with reasonable certainty by radiographic procedures. The smaller congenital pericardial cyst or diverticulum usually has a characteristic "tear-drop" configuration in the lateral view, which serves to identify it. An omental herniation through the right foramen of Morgagni can nearly always be identified by the elevation of the transverse portion of the colon and by air in the hernial sac following pneumoperitoneum.

(Of our 16 proved cases, 12 were either congenital pericardial cysts or omental herniations, and of these, 10 could be diagnosed with reasonable certainty by roentgenologic procedures alone.)

Large pericardial cysts and diverticula, and hernial sacs which fail to fill with air because of adhesions obliterating the neck of the sac, cannot be diagnosed with cer-

tainty by roentgenologic procedures alone. In these cases, a cystic structure may be suspected if definite changes in shape occur with respiration. Omental hernias may be suspected if there are alterations in the position of the transverse colon.

If none of the above roentgenologic criteria are demonstrable, one is probably dealing with a mass in the third classification (*vide supra*) or with an atypical mass of classification A or B. Any further roentgen procedures should be directed toward determining the structure from which the mass arises. Often an etiological diagnosis cannot be established without surgical exploration.

NOTE: We are indebted to Dr. Israel Berger for the Lawson VA Hospital cases used in this communication.

Emory University Hospital
Emory University, Ga.

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SUMARIO

El Diagnóstico Diferencial de las Tumefacciones del Angulo Cardiofrénico Derecho

El diagnóstico diferencial de muchas tumefacciones del ángulo cardiofrénico derecho puede establecerse con bastante certeza por medio de procedimientos radiográficos. Los más pequeños quistes o divertículos pericardíacos congénitos suelen mostrar una típica configuración en "lágrima" en la vista lateral, que sirve

para identificarlos. Una hernia epiploica a través del agujero derecho de Morgagni puede identificarse casi siempre por la elevación de la porción transversa del colon y por el aire contenido en el saco herniario después del neumoperitoneo.

Los grandes quistes y divertículos pericardíacos, y los sacos herniarios que no se

llenen de aire, por tener adherencias que obliteran el cuello de los mismos, no pueden diagnosticarse con certeza a base de los procedimientos roentgenológicos exclusivamente. En esos casos, cabe sospechar un saco quístico si se observan cambios de forma al respirar. Pueden sospecharse hernias epiploicas si hay alteraciones en la posición del colon transverso.

Si no puede observarse ninguno de los patrones mencionados, los ulteriores procedimientos roentgenológicos se encaminarán a determinar el órgano donde tiene su origen la tumefacción. A menudo no

cabe establecer el diagnóstico etiológico sin una exploración quirúrgica.

De 16 casos comprobados que han observado los AA., 12 fueron bien quistes pericardiácos congénitos o hernias epiploicas; 10 de éstos pudieron ser diagnosticados con bastante certeza por medio de procedimientos roentgenológicos por sí solos. Cuatro casos constituyeron un grupo variado, comprendiendo un carcinoma del timo, un lipoma asentado en el timo, un quiste del mediastino anterior y una rotura traumática del diafragma con hernia del hígado.



Upright Cholecystography Using the Fluoroscopic Spot-Filmer with Graded Compression¹

MORTIMER LUBERT, M.D., and GEORGE R. KRAUSE, M.D.

THE USE OF A fluoroscope to provide both a horizontally directed roentgen-ray beam and graded compression in cholecystography has been recommended for many years. Åkerlund (1) described this procedure in 1933; subsequently Ettinger (2) and more recently Greenwood

the lateral decubitus position (Kirklin, 4), using the Potter-Bucky diaphragm. Both methods are difficult and time-consuming, requiring exacting technic and sometimes special equipment. The examination is often unsatisfactory and must be repeated. Because of the disappointing quality of

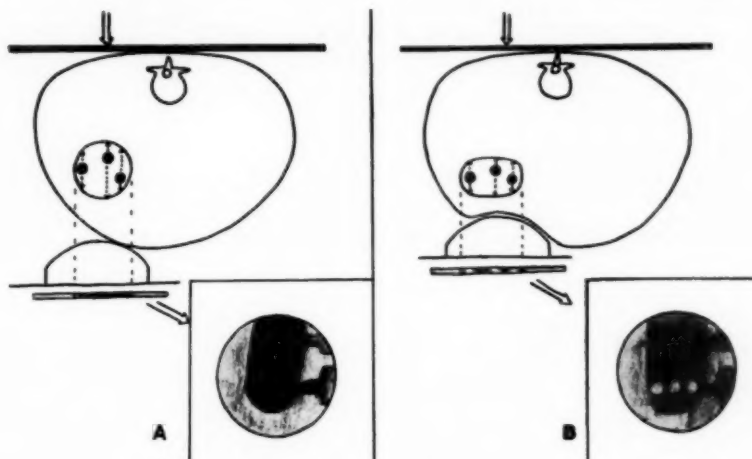


Fig. 1. Diagrammatic representation of compression effect in the upright fluoroscopic spot method (horizontal section through the gallbladder). Undoubtedly, in most instances, stones can be detected on upright films without compression, provided the gallbladder can be projected free of gas and bone shadows. However, when the gallbladder shadow is dense and/or the stones are small and few, compression may be absolutely essential to the detection of stones.

A. No compression. Ratio of contrast medium to stone diameter is high. B. With compression. Ratio of medium to stone diameter is low.

and Samuel (3) have called attention to this method. It is our purpose to reaffirm and illustrate its diagnostic worth and to emphasize the ease with which it can be accomplished.

The value of horizontal-beam cholecystography and the physical and physiological principles which are behind it have been generally accepted. In practice, however, there is considerable variation. Most radiologists favor either the upright or

the films and the time consumed in making them, many radiologists do not employ either technic routinely. Use of the fluoroscopic spot-filmer, now almost universally available, not only removes most of the objections to the upright or decubitus Bucky film, but offers in addition certain advantages, among which is the technic of graded compression.

The introduction of new cholecystographic media which frequently yield

¹ From the Department of Radiology, Mount Sinai Hospital, Cleveland, Ohio, Dr. Herbert A. Mahrer, Director. Presented as an exhibit at the Thirty-eighth Annual Meeting of the Radiological Society of North America, Cincinnati, Ohio, Dec. 7-12, 1952.

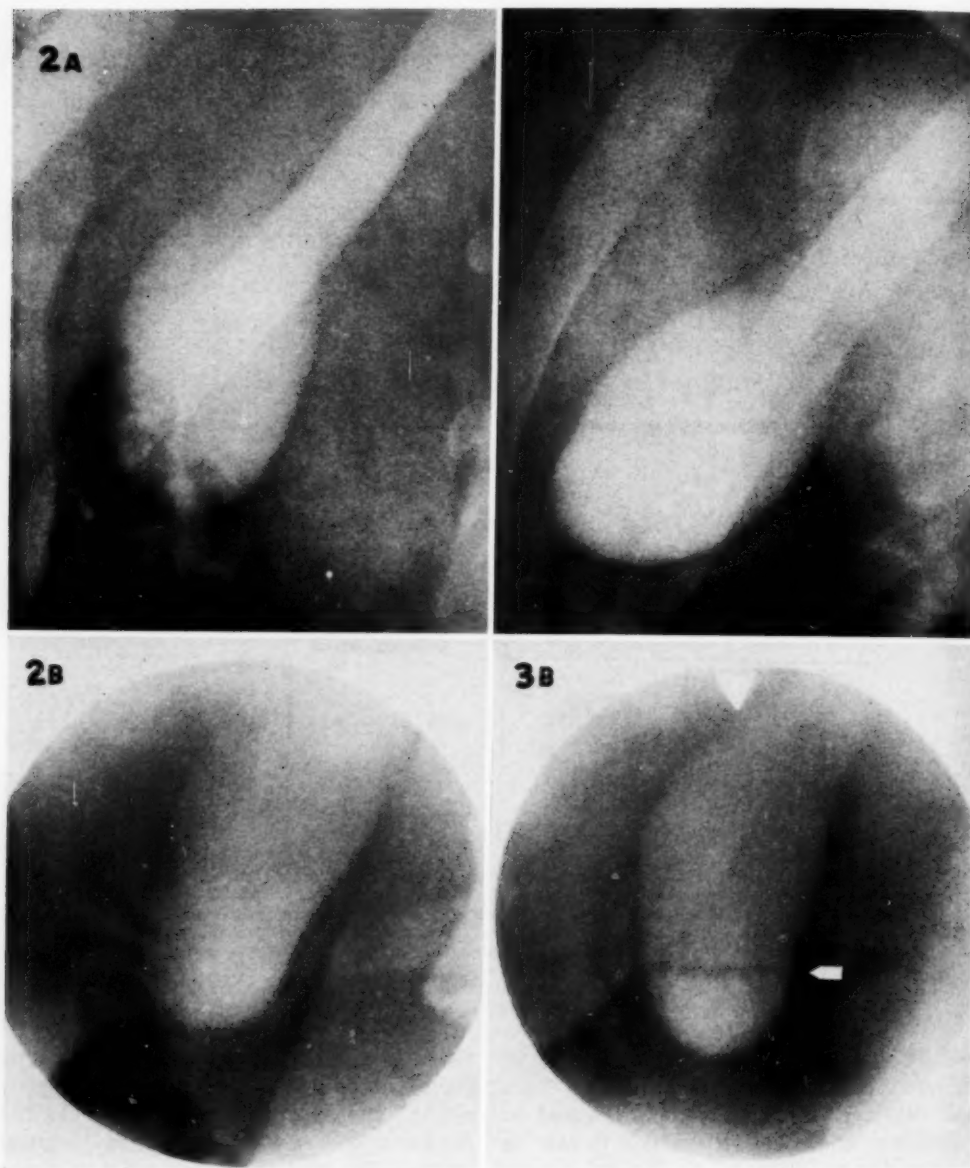


Fig. 2. A. Conventional prone film, representative of several, in all of which colonic gas shadows partially covered the gallbladder. The extent of interfering gas shadows is often much more marked.

B. The upright compression spot film illustrates displacement of the gallbladder away from the gas shadows. Note that the quality of the spot film compares favorably with the Bucky film.

Fig. 3. This case is typical of a number in our files. A. The conventional film (one of several taken) appears to be normal, even in retrospect.

B. The upright compression spot film reveals a layer of radiolucent stones (arrow).

overly dense shadows makes mandatory further improvement in technic. Stones may be hidden within the dense shadow of

the gallbladder and be revealed only by using the horizontal beam *combined with compression* (Fig. 1), a method which is

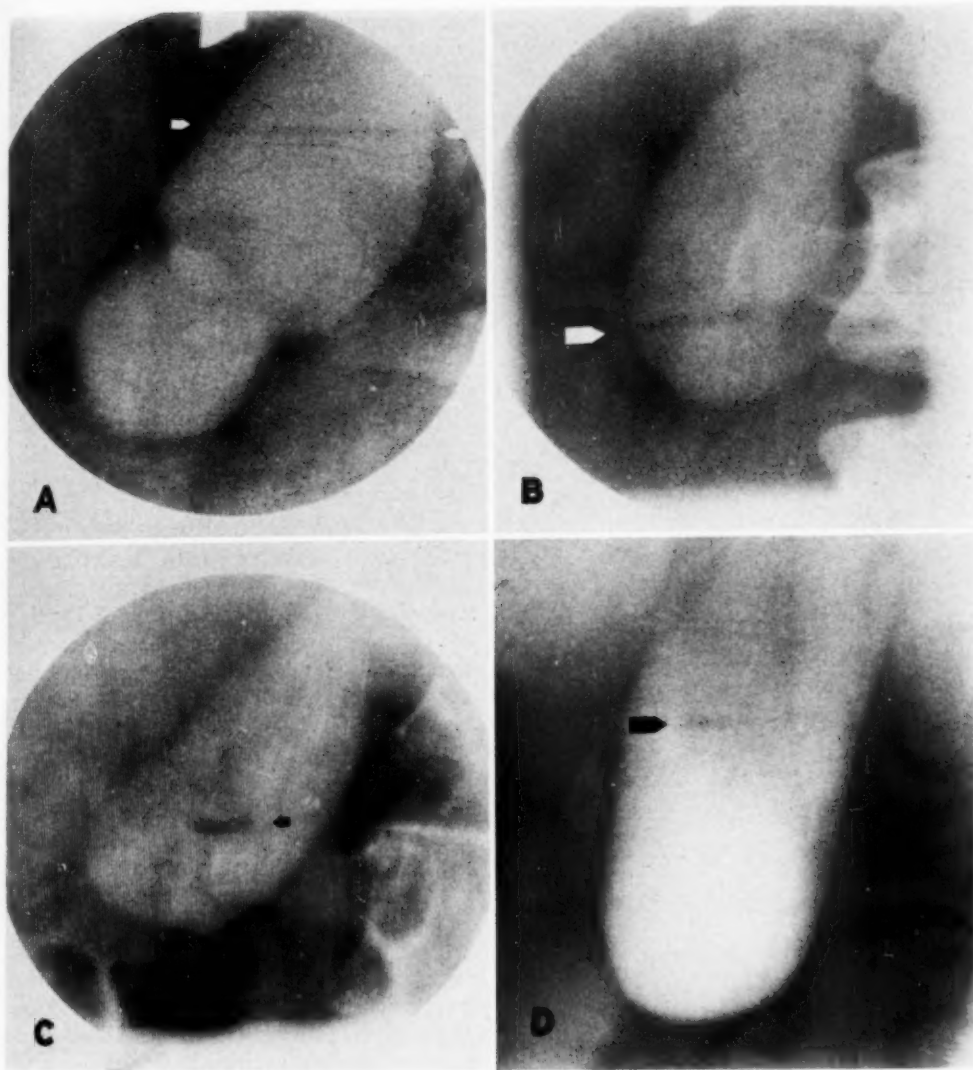


Fig. 4. Fluoroscopic spot films on four different patients. Each shows layering of stones (arrows), complete in A and B and incomplete in C and D. In none of these cases was it possible to make a definite diagnosis of stones on technically good conventional prone films.

analogous to mucosal studies in gastrointestinal radiology. In cholecystography, however, it is difficult and it may be dangerous to attempt to control the density of the gallbladder shadow by varying the amount of contrast material administered. Some apparently normal gallbladders do not cast dense shadows, so that with insufficient medium they may

fail to be visualized and be erroneously classified as "non-functioning." Fluoroscopic technic with compression permits maximum dosage of contrast material for positive identification of the gallbladder, followed by thinning of the shadow (with pressure) for direct demonstration of the pathologic findings (stones) (Figs. 3-6).

In addition to these virtues, the use of

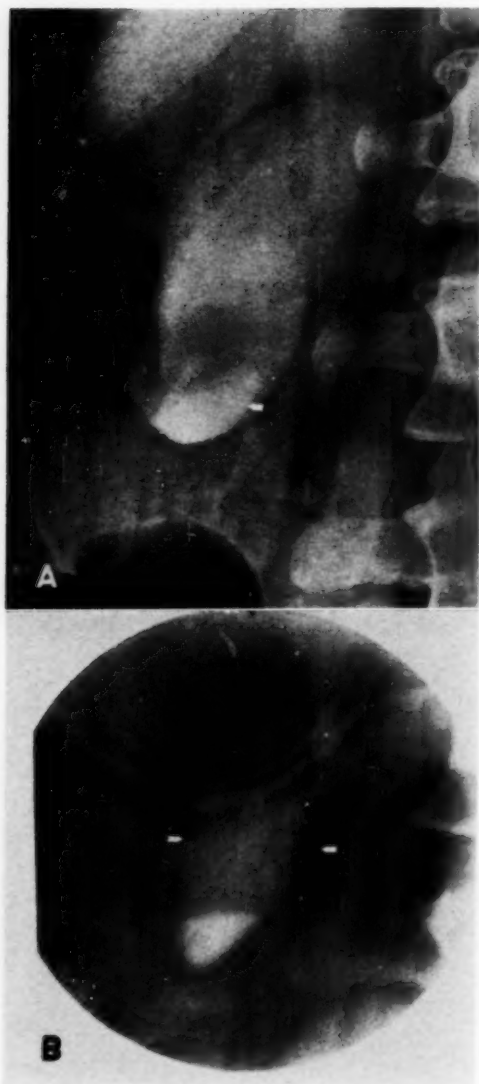


Fig. 5. A. Prone film revealing concentration of medium without evidence of stones. A more dense shadow in the fundus does not have the appearance of a stone. It resembles a phrygian cap.

B. Compression spot film reveals that the density in the fundus is amorphous and conforms in shape to the fundus. It represents milk-of-calcium bile. (A preliminary film without contrast medium would also reveal this, but since this requires an extra visit by the patient, it is not routine in many institutions.)

the fluoroscope permits several views of the gallbladder to be taken in rapid succession, in various degrees of rotation and tilt. Overlying structures, gas, and

the opaque bowel residues of the newer contrast media may be compressed or pushed out of the way (Fig. 2); the gallbladder itself may be displaced into a more favorable location. The ribs, the vertebrae, and bony pelvis may be avoided under direct inspection. The ease with which even a faint gallbladder shadow can be located is surprising, but only rarely can the pathologic findings be identified during the screen examination. The films are usually definitive.

We secure upright compression spot films in all cases in which the gallbladder is visualized unless obvious stone shadows are present in the routine views. For average patients, the exposures are 0.1 to 0.2 second at 65 to 75 kv. and 100 ma. Lower voltages are preferred because compression tends to diminish contrast between the gallbladder and the surrounding tissues. The short exposure time, immobilization by the pressure cone, and the small field size enhance detail and compensate for the lack of a Potter-Bucky diaphragm. Excellent films may be obtained with stationary anode tubes; obviously a rotating anode tube will improve detail, but its use is not critical. A grid is usually not needed. Indeed, if its lines are horizontal, it may sometimes interfere with the identification of very small stones.

Following the conventional prone films, the examiner (who must be dark-adapted) takes four views of the gallbladder with varying degrees of rotation and pressure. If the gallbladder is low, it may be pushed up by manual pressure outside the field or by the pressure cone. With a medially placed gallbladder, tilting the patient to his left is of great help. A favorite clear space is the one just lateral to the lumbar spine, overlying the apex of the right psoas muscle. Here both the colon and the descending duodenum are usually avoided and the pressure on the gallbladder is most effective (Figs. 4A and C, 5B, 6A).

Upright films may be made immediately following the prone films. It is not necessary to wait until the bile "settles." Campbell and Burton (5) have demon-

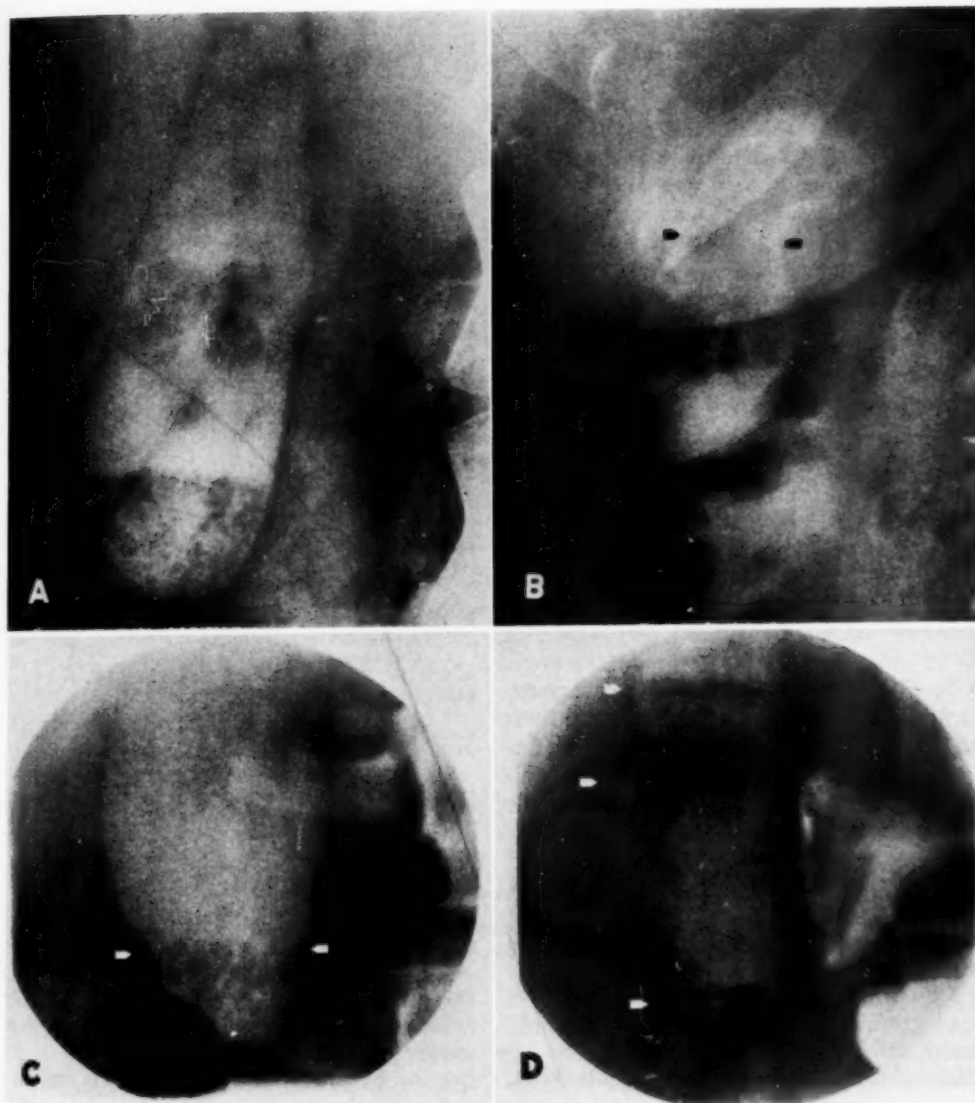


Fig. 6. Examples of radiolucent stones which seek different levels in the gallbladder. The size of the stone has no effect on its position. The relation of the specific gravity of the stone to that of the contrast medium-bile mixture is the important factor.

- A. Small stones sink to the bottom. Large ones float.
- B. Stones of varying size all rise to the top. Arrows mark the wall of the gallbladder.
- C. Many small stones sinking to the fundus (arrows).
- D. Stones are present in three separate layers (arrows) and therefore each group must have a different specific gravity. A partial septum extends across the gallbladder between the upper two layers of stones.

strated that stratification of bile is persistent and not easily disturbed, even *in vitro*. In our experience, change in position does not alter layering. After a fat meal stones may change in position but are still

easily identified. The gallbladder examination may be followed by an upper gastrointestinal series, and the relation between the gallbladder and duodenum may be studied directly.

Occasionally upright spot films with compression will demonstrate stones in the gallbladder which are not otherwise detectable (Figs. 3 and 4), but the greatest value of the method lies in the fact that doubtful cases can in most instances be converted to clear-cut negative or positive diagnoses without a repeat examination. The use of pitressin and cleansing enemas following the routine conventional films can be eliminated almost completely. The reduced number of re-examinations is an economy and convenience both to the patient and the radiologist.

It is conceded that the use of the fluoroscope in cholecystography does carry the possibility of further exposure of the radiologist to ionizing radiation, a hazard in any fluoroscopic procedure. However, the exposure time is very brief. The usual protective measures should always be used.

CONCLUSIONS

1. With the fluoroscopic spot-film device it is possible to obtain multiple films of the gallbladder, quickly and conveniently. To the virtues of horizontal-beam cholecystography are added the

advantages of graded compression under direct vision, so that interfering shadows are reduced to a minimum.

2. Optimum utilization of the more dense cholecystographic media is achieved by neutralizing some of their inherent drawbacks.

3. The reduction in the number of re-examinations represents a considerable economy in time and materials.

NOTE: We would like to express our appreciation to Mr. William Stevenson and Mr. Robert Newhouse of the Department of Photography, Mount Sinai Hospital, for the reproductions.

1800 East 105th St.
Cleveland 6, Ohio

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SUMARIO

La Colecistografía Erecta Usando el Aparato de Roentgenoscopia Instantánea con Compresión Graduada

Con el aparato roentgenoscópico de radiografías instantáneas es posible obtener, en forma rápida y conveniente, radiografías múltiples de la vesícula biliar en varios grados de rotación e inclinación. A las virtudes de la colecistografía con haz horizontal se sobreponen así las ventajas de la compresión graduada bajo visión directa, de modo que se reducen a un mínimo

las sombras obstructoras. Además, resulta posible la utilización óptima de los medios colecistográficos más espesos, dado que se neutralizan algunos de los inconvenientes de que adolecen.

Con ese procedimiento, no se necesita tan frecuentemente la repetición del examen, lográndose así una economía considerable de tiempo y de materiales.

Direct Measurements and Isodose Calculations in Radium Therapy of Carcinoma of the Cervix¹

GILBERT H. FLETCHER, M.D., JOHN A. WALL, M.D., FERNANDO G. BLOEDORN, M.D.,
ROBERT J. SHALEK, M.A., and PETER WOOTTON, B.S.

UNTIL RECENTLY, radium treatment of carcinoma of the cervix was prescribed in terms of milligram hours. Although such a designation is meaningless on radiobiological grounds, considerable experience has been acquired to guide treatments on a clinical basis. The amount and distribution of radium, both for the uterine tandem and the vaginal applicators, were empirically established by the pioneer Radium Centers. Through the years, cure rates improved and radiation damage decreased. Better results and less damage could still be obtained, however, by the same well developed techniques, with a knowledge of the energy absorbed at the various points in the pelvis.

The total amount and distribution of radium in the uterine tandem and vaginal applicators and the shape and design of the applicators might be changed to advantage. Without a knowledge of the radiation volume distribution, any change from a technic established on clinical experience is likely to become an almost entirely new technic, since a new applicator, changing the geometrical relationship of the radium sources, modifies the distance between the radium and the mucous membrane, rectum, and bladder. The number of milligram hours suitable for an established procedure may not be appropriate for a new system.

Scientific radium therapy of carcinoma of the cervix must be based on a knowledge of the volume distribution of the dose within the pelvis, with a view to (1) designing applicators producing the largest possible volume of adequate radiation in each of the common directions of spread of the disease, namely, the uterine body, parametria, and perivaginal tissues; (2) determining the doses tolerable for vital

organs such as the bladder and rectum, the sites of most of the serious complications.

It must, however, be kept in mind that the results obtained in the best Radium Centers without the help of dosimetry, and based only on long clinical experience of the individual radiotherapist, have yet to be surpassed. It would be decidedly a retrograde movement to accept the tagging of physical data to various points of the pelvis as replacing individual clinical experience and skill in the handling of radium. Flexibility and adaptability of the radium system to the anatomy and type of disease encountered should not be sacrificed in the interest of easier dosimetric procedures, the accuracy of which is often more apparent than real. Dosimetry gives a base line, helps the new generation of radiotherapists and gynecological therapists to understand the experience of the past, and is a working tool in the use of radium with safety and to its maximum advantage. An exaggerated emphasis on figures and a complacent regard for well filled forms where gamma roentgens appear cannot compensate for the inexperience of the therapist. Better physics and greater accuracy in physical measurements are a necessary trend if associated with extensive clinical experience of the disease and skill in the details of technic. Clinical judgment, which includes the prediction of the likelihood of response and the choice of dose, will always remain paramount in the use of radiation of any kind.

Heyman (2) demonstrated that results improved by more than 30 per cent where individualization of technic, allowed by the use of flexible uterine and vaginal ap-

¹ From the University of Texas, M. D. Anderson Hospital for Cancer Research, Houston, Texas. This study was supported in part by a grant from the American Cancer Society. Presented at the Thirty-eighth Annual Meeting of the Radiological Society of North America, Cincinnati, Ohio, Dec. 7-12, 1952.

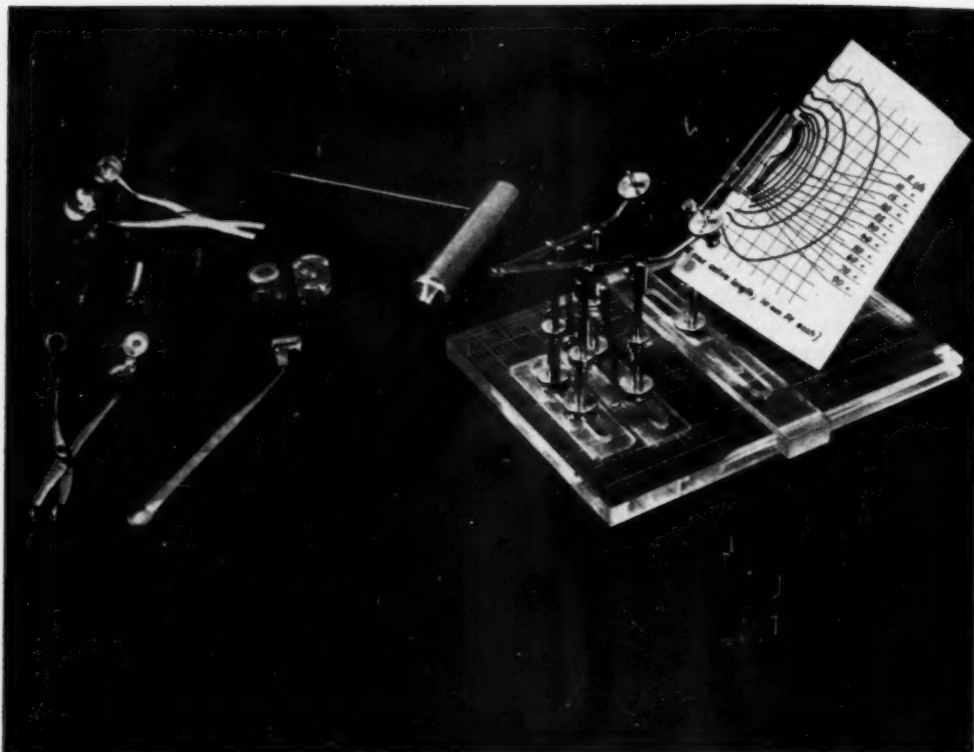


Fig. 1. The colpostats (pair and single), plastic jackets to increase diameter, tandems, clinical probe, and dose-finder are shown; the theory of the clinical probe and dosefinder has been published before. Notice on the isodose curves the sharp gradient of dosage rate in the vicinity of the radium sources. From 1 to 2 cm. it drops from 70 to 30 r/hr.

The radium technic is briefly as follows: Loading depends on the separation, *i.e.*, 15-20, 20-25, and 25-30 mg., respectively, in small, medium, and large cylinders. The uterine tandems, depending upon their length, are loaded with 15, 15-10, and 15-10-10 mg. The uterine loading is somewhat higher (15, 15-10) and the vaginal loading is diminished (15, 20, 25) if the lesion is more infiltrative and if there is no retroversion or extreme anteversion. The application time is determined by the measurements in bladder and rectum, not to exceed 3,500 gamma roentgens to the bladder and 3,000 gamma roentgens to the rectum for each application, if no external irradiation has been given to the mid-line. Applications are made ten days apart. Usually, on subsequent insertions, colpostats of smaller diameter can be fitted. If colpostats and uterine tandems are used separately, the insertions are weekly (three or four). Not infrequently one ovoid only, as large as possible, is used in contracted vaults in one or both the insertions (20, 25, 30). The total treatment time for both tandem and colpostat ranges between 100 and 144 hours.

plicators, was employed. Dosimetric procedures should not aim at treating theoretical points or creating ideal geometric volume distributions that may be unrelated to the anatomical spread of the disease (7). Rather the dosimetry should be an aid in the adaptation of treatment to an infinite variety of anatomical set-ups.

Following the definition of the gamma roentgen and the calculation of isodose surfaces around linear radium sources, systems of radium dosimetry were estab-

lished. The Paterson and Parker system, founded on the conception of the mean dose within an irradiated volume, is not applicable to gynecological intracavitary radium therapy, which involves a T-shape arrangement of the radium sources. The dosage rate decreases rapidly from around the radium sources toward the periphery of the pelvis, so that there is no mean dose anywhere and no point that is representative of an area.

Before entering into a study of the prac-

tical significance of any system of dosimetry in radium therapy of cancer of the cervix, it should be recalled that near a radium source the gradient of the dosage rate is very steep (see isodose curve of Fig. 1) and that a small change in distance brings a large change in dose. Also, in dealing with anatomical organs, especially in the presence of malignant disease, no average quantitative morphology can be expected.

In view of these considerations, one must approach the problem with a conception of the obtainable accuracy compatible with clinical significance and practical usefulness. A dosimetric procedure should meet the following requirements:

- (1) Insure that the primary disease in the cervix and fornices and its immediate extensions into the paracervical triangle are adequately treated. This implies the determination of the volume distribution in a plane passing through the fornices and the paracervical triangle. The supplementary external irradiation should then be planned so that the central slab of tissue which has already been adequately treated is no longer irradiated.
- (2) Guide treatments in such a way that the bladder and rectum, which are the organs most commonly damaged, are not overtreated.
- (3) Determine the dose received by the various lymph node groups. This should be added to the dose given to the pelvic wall by external irradiation.

A few comments on the anatomical relationship of the radium sources to vital organs will be helpful in the discussion of the technic of dosimetry:

Bladder: The bladder is a distensible organ which, when filled, is a spheroid with a flat base and, when empty, is like a tent collapsed on its base. Books on anatomy and urology do not give much information as to the area and dimensions of the base of the bladder. It has been

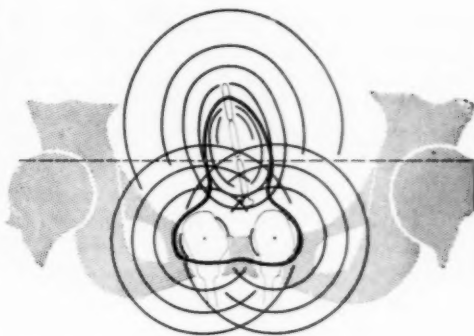


Fig. 2. Lateral throw-off computations.

The plane for study is defined by the center of the vaginal applicators and a point 2 cm. above the flange of the tandem, *i.e.*, approximately at the level of the internal os. Isodose curves, enlarged to allow for the average magnification of the anteroposterior localization films, are overlaid directly on the films. The contributions from the various sources are added to yield a compounded 3,500 gamma roentgen curve (7,000 gamma roentgens total treatment) and, also, the dose every 0.5 cm. on the frontal line passing through the internal os laterally. No allowance is made for the angulation of the plane to the colpostat, since the equatorial 90° curves do not change much with small changes of angle. The projection of the tandem contribution on the plane is made easy in practice by sets of curves in the plane prepared for each loading of the tandem and with 15° increments of angulation between the plane and the tandem. The angle is determined from the lateral films and allows the choice of a standard curve to be used in the manner described above. If there are more than two insertions, the curves for each insertion are compounded in a similar fashion.

The heavy lines drawn on all the lateral films reproduced in this paper represent the plane passing through the paracervical and paravaginal tissues. The angle made by this plane and the axis of the tandem is indicated.

assumed in radium dosimetry that, if the bladder is kept empty by an indwelling catheter, it contracts around the small filled bulb and the base and posterior wall are adequately identified by a radiopaque medium placed in the bulb. We have taken measurements on autopsy material and in the knee-chest position with the "Kelly" cystoscope. The length of the urethra has been found to be 3 to 4 cm. and the distance from the bladder neck to the urethral orifices 2.5 to 3 cm. These data agree with those of the textbooks. The distance from the urethral meatus to the posterior wall has been found to be 9 to 11 cm. At autopsy, with the body in supine position, one can pass a sound in an empty bladder for a distance of about

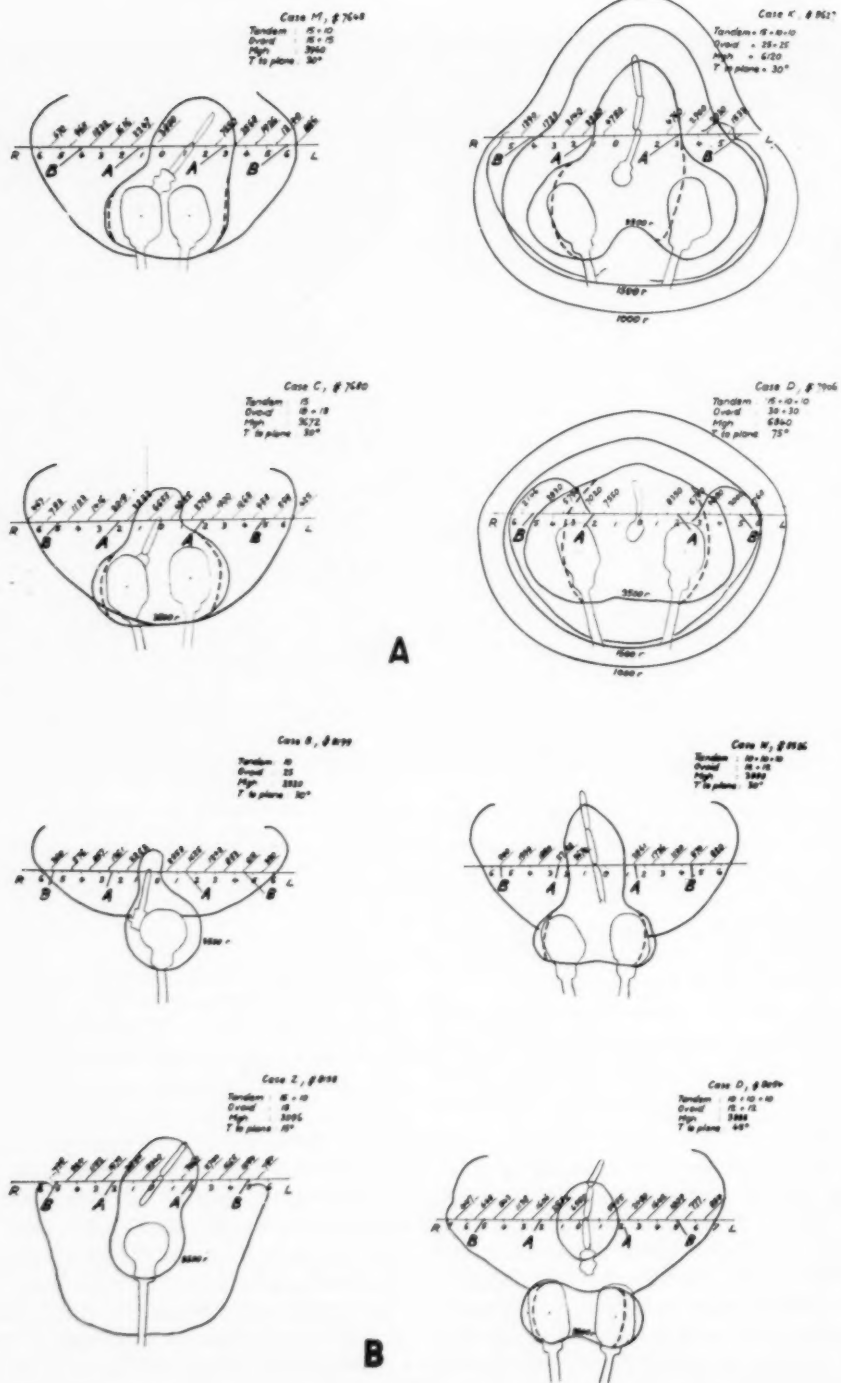


Figure 3
(For legend, see opposite page.)

10 cm. before a bulging of the bladder wall is apparent. From this, one can infer that the base of the bladder is not "a point" but a "surface," with an average length of about 6 or 7 cm. This is usually a minimum, due to the fact that the base of the bladder is closely attached to the whole length of the anterior vaginal wall. The wall of the vagina and the intimately attached bladder base are stretched out by the vaginal applicators and the packing. The base of the filled bulb of the Foley catheter identifies only the area adjacent to the bladder neck. Sodium iodide must be injected directly into the bladder to visualize its entire base. This is essential, since the contribution of the uterine tandem is greatest in the more distal areas of the base. In an anteflexed uterus, a very hot spot can be present 8 to 10 cm. from the urethral meatus.

Rectum: The rectum and rectosigmoid are even less "a point" than the bladder. This viscus is a flabby, cylindroid tube with a spiral axis, changing diameter and position depending upon the amount of gas and feces present. Rectal ulcerations and rectovaginal fistulas, always on the anterior rectal wall, are usually due to an overdose of radiation to the anterior wall at the level of the posterior fornix behind the radium in the vagina. As is true of the skin and other tissues, the severity of damage is not only a function of the dose, but

also of the surface irradiated. A knowledge of the dose at one point is not enough. One must know the doses on a strip along the rectovaginal septum and rectosigmoid up to the level of the isthmus. That strip of anterior rectal wall receives the maximum doses and is the site of almost all the rectal ulcerations. Higher in the rectosigmoid the diffuse fibrosis responsible for rectosigmoidal strictures is due to a more generalized damage to the pelvic vessels.

The anterior rectal wall is usually visualized on a lateral film by the presence of gas shadows or by means of a thick barium paste smeared on the wall. A gas shadow, however, if present in the rectum and sigmoid, is inadequate for determination of the anterior wall. Packing will protrude inside the dilated lumen and the gas shadow in the lateral grooves will give a false localization. If the vagina is elastic and the application correct, the vaginal radium is then so high that the finger cannot reach its level to smear the wall with barium (Fig. 5C and Fig. 6A). If packing has been used, it protrudes into the lumen, making a groove on each side. The barium in these grooves projects on the lateral film closer to the applicator than the mucosa behind the packing. Errors of 1 cm. in the location of a point bring differences of 50 to 100 per cent in doses. Injection of a sufficient amount of thin barium paste (2 ounces) in the rectum is

Fig. 3. A. Eight examples of volume distribution in a plane passing by the centers of vaginal cylinders and internal os. This plane transects the paravaginal and paracervical areas. The influence of length of tandem and separation of vaginal cylinders on the size of the area of adequate irradiation (3,500 gamma roentgens for each insertion, 7,000 gamma roentgens for both insertions) is obvious. The steep fall-off of the dose along the frontal line passing by the internal os illustrates once more the difficulty of dosimetry in the vicinity of the radium sources. The inadequacy of intracavitary radium therapy is glaring if one does not have a reasonably good distribution of the radium sources (Fig. 3B, Case B). One notices the asymmetry in relationship to the mid-line. In cases of mid-position of the uterus, the lateral throw-off at the level of the internal os into the paracervical triangle is highly dependent upon the length and loading of the tandem. In anteflexed or retroflexed uteri, Case D, the paracervical triangle is closer to the vaginal sources and the width of the 3,500 gamma roentgen zone at the level of the internal os is greater.

B. Case D shows that, if the colpostat is not high enough in the vault, there may be an "undertreated area" on the cervix itself and on the fornices. In this instance, a single cylinder should have been used to fit higher in the vault or/and a stronger source in the cervical canal. Fitting of proper colpostat and tandem and flexibility in radium loading are most essential in preventing inadequate treatment to the primary lesion.

In planning the external irradiation to the parametria, one must take into account the medial shift of paravaginal tissues after removal of the distending colpostat. The dotted lines show the corrected 3,500 gamma roentgen isodose curves drawn with cylinders in contact, *i.e.*, without distention of the vagina. The tissues in the vicinity of the 1,500 or 1,000 gamma roentgen curves are inappreciably affected by the lateral pressure of the colpostat.

One notices that the doses at Points A and B are not always symmetrical. They also differ in several instances from doses calculated from tables similar to those used in other institutions, where a practice has been made of calculating doses at Points A and B. This discrepancy is to be expected if one does not have a single-piece applicator.

A
SUMMARY OF RADIUM TREATMENT

Name K. M. No. 8627 Color W Sex F Weight _____

Diagnosis Med. Adeno + Squamous Cell Ca Cervix Treatment Planned Radium and Lymphadenectomy when Stage I (pos. early I) last application of Ra removed

1. CYTOLOGICAL TREATMENT (SEE OVER FOR INTERSTITIAL TREATMENT)

I		II		III		BLADDER		RECTUM		
						T	T+D	T	T+D	
						I	3040 (m)	5403 (m)	675 (7)	1405 (17)
						II	590 (8)		510 (n)	
						III		920 (8)	1470 (14)	
								Ant. Fornix	Post. Fornix	
								4709	2320	

				UTERUS		VAGINA			
INSERTION	DATE	BY	TIME	APPLICATOR	MG.	APPLICATOR	MG.		
I	7/14/52	F.B.	7:24	3" Tandem	2520	Large Ovoids	3600	TOTAL MG.	11,160
				18-10-10		2.5-2.5		DOSE (r gms.)	
II	7/24/52	GAF		3" Tandem	2160	Empty Ovoids	-	POINT A	7,752
				10-10-10				POINT B	2,650
III	8/14/52	GAF		-	-	Medium Ovoids	2400	VAG. VAULT	
						20-20		BLADDER	
								RECTUM	
								LAT. ASPECT OF	
								PARAMETRIA	
					TOTAL	4680	TOTAL	6000	

B

Lymphadenectomy
(3rd Application)

Name K. M. No. 8627 Date: 8/5/52

Measured		External Iliac Principal Gland (Obturator N.) Obturator Foramen Hypogastric	

C

E.M., 8627

	BLADDER				TOTAL	RECTUM				TOTAL
	I	II	III	IV		I	II	III	IV	
1 cm										
2 cm										
3 cm	780	234	346		1360	780	147	590	292	1217
4 cm	995	320	440		1755	1020	234	665	365	1689
5 cm	1405	400	510		2315	1265	225	1030	510	2000
6 cm	2025	390	650		3065	1390	216	1470	650	2736
7 cm	2390	468	790		3648	1405	254	1990	1020	2769
8 cm	3080	522	920		4522	1378	277	2570	1458	3383
9 cm	4320				4365	277	270	2600		3347
10 cm	4400				4400	220	442	2420	1670	3332
11 cm								410		
12 cm										
Ant. F.	4707									
Post. F.	2320									

No packing under ovoids;
Packing around parametria

No packing at all
No packing under ovoids;
Packing only around parametria

Fig. 4. A. The working radium form, where sketch of radium system and amount of radium are recorded for the successive insertions. The doses at Points A and B are calculated from tables similar to those used in the Manchester system. The treatment is not guided according to those figures but it was thought that this information ought to be kept for the eventual purpose of comparison.

B. Form on which direct readings are recorded for each insertion. In this instance, the radium system was very high (Fig. 5B and C), the vaginal radium being at the level of the principal node (obturator node). At the time of removal of the radium of the third insertion, direct readings were taken at the various lymph node group sites while the radium was still *in situ*.

C. Form for totaling the rectal and bladder doses from each insertion.

accurate only if special stereoscopic techniques are used (3).

Paracervical Area and Parametria: The paracervical area and parametria are between the radium and the pelvic wall. It is difficult to talk of tolerance of the paracervical triangle because the dosage rate can vary by a factor of two or three in a distance of less than a centimeter. Because of rapid variation of dose rate, no point is representative of the "paracervical triangle." The importance of Point A came from its association with the crossing of the ureter and the uterine artery and the possible damage to these two structures. It is a point geometrically related to the uterine tandem (8) (2 cm. from the flange, and then 2 cm. laterally) and has no fixed relationship to the above-mentioned anatomical structures. The important information is the determination of the zone of adequate radiation (let us say 7,000 gamma roentgen isodose surface). The 7,000 gamma roentgen isodose curve produced by the cross section of that surface with a plane passing through the paracervical triangle and the paravaginal tissues is adequate for practical purposes, determining the width of the central slab of tissue which should not receive additional external radiation (Fig. 3). This plane is determined by the centers of the vaginal applicators and the internal os (approximately 2 cm. from the flange of the uterine tandem) Fig. (6A and B). Knowledge of the width of the central slab of tissue which should receive no additional external radiation is essential in the planning of parametrial portals (Fig. 3). This width is not critical to the millimeter and a stepwise increase in the separation of the parametrial fields is useful in providing a safety margin. The medial shift of paravaginal and parafoveolar tissues, after the removal of the distending radium applicators, should be taken into account in the determination of the separation of the x-ray fields.

Pelvic Nodes: The location of the principal groups of nodes is not critical for two reasons: (a) The variation in location of the nodes produces a small error in the

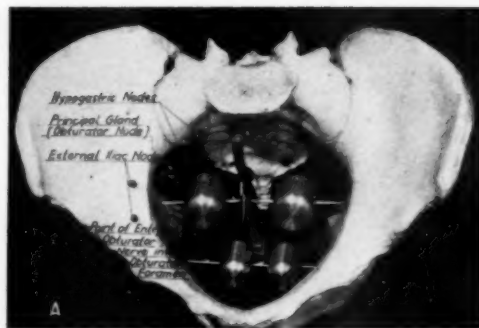


Fig. 5A. Small balls have been pinned on a bony pelvis to identify node groups according to lymphadenectomy findings. Two radium systems have been reconstructed in space, showing the difference in relationship to pelvis and nodes.

calculated dose since the distance from the radium sources is relatively large. (b) The dose from the radium is low, and external irradiation is the important factor. Thus an indication of the range of the gamma-ray dosage can be a useful guide.

Studies during extraperitoneal lymphadenectomies have established the following relationship to the bony pelvis: The principal node (obturator node group) is somewhat higher than the center of the inner aspect of the acetabulum; the hypogastric group is at the same level as the principal node and 3 or 4 cm. posteriorly; the external iliac nodes are strung all along the upper aspect of the pelvic brim (Fig. 5A). Point B is superimposed upon pelvic nodes only in very high insertions allowed by a distensible vagina. As a rule, Point B is several centimeters (3 to 5 cm.) below the principal node and hypogastric nodes, the distance being dependent on the height of the radium system, which in turn is a consequence of the mobility of the uterus, elasticity of the vault, and tightness of packing.

Cervix and Vault: These areas tolerate extremely high doses and the margin of safety is great. Doses on the cervix and vault are determined by the design of the colpostat and will never be excessive (20,000 gamma roentgens maximum) if there is sufficient radium-mucous membrane distance, as the dose on the vault is

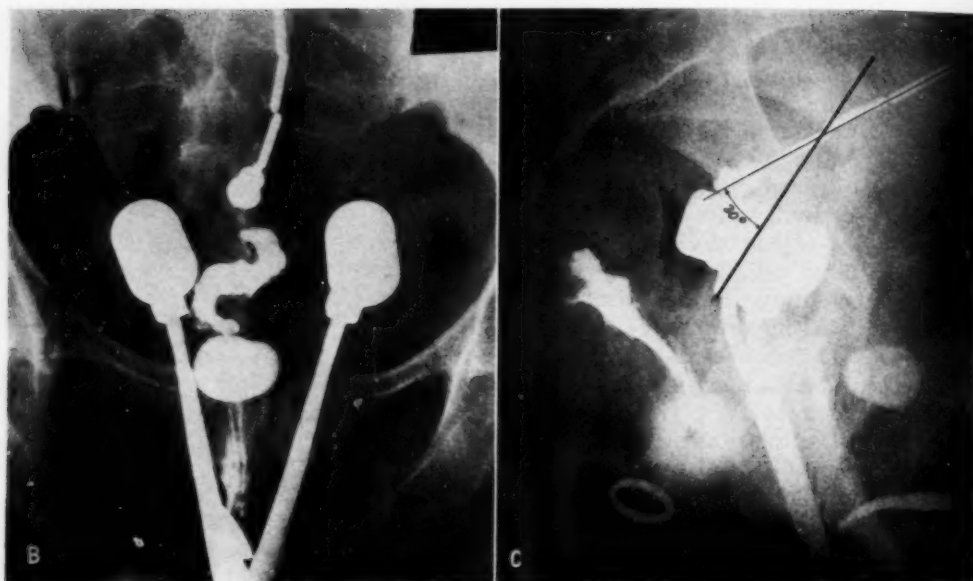
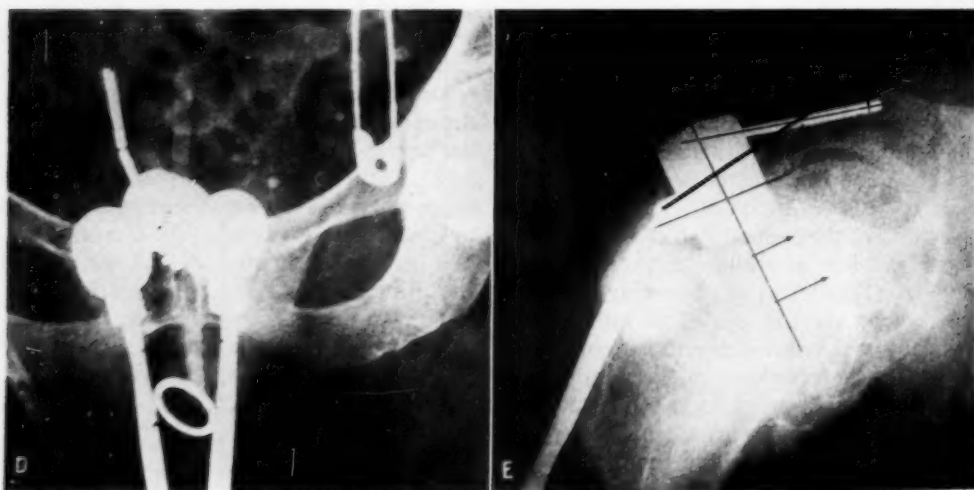


Fig. 5B and C. Large ovoids with 4 cm. separation, 25, 25 mg. sources, and 15-10-10 milligram sources in tandem. Sodium iodide in bulb of Foley catheter, ring taped to anal margin, barium smeared and injected in rectum (note inadequacy of procedure to visualize anterior rectal wall). The volume distribution is Case K, Fig. 3A.

The radium system is high, the ovoids being at the level of the principal node. In view of this, the patient was treated with three insertions, the last with ovoids only, and a lymphadenectomy was performed at the time of removal of the radium. The doses to principal node and hypogastric nodes are about twice the average for vaginal radium alone. Radiographs of the third insertion show that the position of the colpostat is as high as in the first one.



Figs. 5D and E. Small ovoids with 1 cm. separation (15, 15) and tandem (15-10). The radium system is low. The case was not suitable for lymphadenectomy. It is evident that the contribution to the nodes would have been very low.

practically the dose at the surface of the colpostat. Calculation of doses for the so-called "cervical point" is meaningless, due

to the extremely steep gradient; no one point is representative even of a small volume.

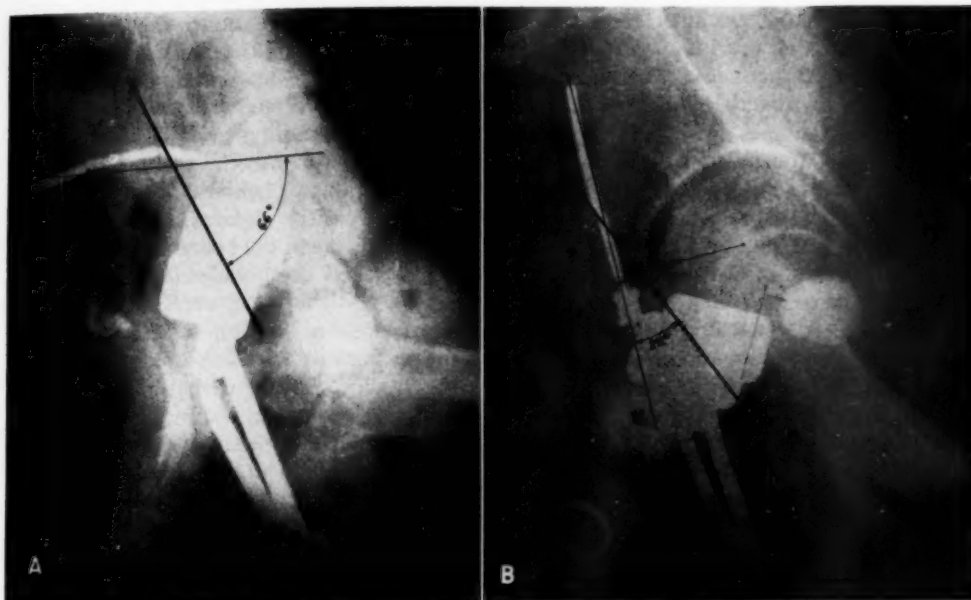


Fig. 6. A. Tandem, 15-10-10 mg., and large ovoids, 25, 25 mg. with 3 cm. separation. Despite third-degree retroversion, the maximum rectal dose is 2,980 gamma roentgens (seventy-two hours), at 10 cm. from the anal margin, with a strip of 6 cm. above 2,000 gamma roentgens. Barium or gas shadow is in this case of no help in locating the "hot spots" on the anterior rectal wall.

B. Tandem, 15-10-10 mg., and small ovoids, 18, 18 mg. with 1 cm. separation. The rectal dose was 5,390 and 5,430 gamma roentgens at 9 and 10 cm., with at least 8 cm. above 2,000 gamma roentgens (the probe could not be inserted more than 11 cm. and the readings were still 3,630 gamma roentgens). The radium was left only twenty-four hours. Three insertions were used and, despite changes in loading and size of tandem and colpostat, the maximum rectal dose was 7,096 gamma roentgens for a total of only 7,584 milligram hours.

TECHNICS OF DOSIMETRY

There are four procedures which can be followed:

(1) *Precalculated tables* are made for several theoretical arrangements of radium sources, varying the length and loading of the uterine tandem and the distribution and loading of vaginal radium. From these, rectum and bladder doses are determined, assuming average distances in the median sagittal plane. The same procedure is used for such points as A and B. If one is dealing with a single-piece applicator, doses at A and B are obviously accurate, as A and B are determined by the rigid system of reference of a one-piece applicator. Otherwise, if the uterine tandem and vaginal applicators are separate, the dose at A and B will vary with each application depending upon the geometrical relations (degree of flexion, lateral shift of the uterus, etc.)

Furthermore, the radium system occupies a wide range of positions inside the pelvis, depending upon packing, the length and position of the uterus, the length and width of the vagina, and the flexibility and elasticity of the tissues. The assumption of a constant distance from the radium system to the rectum, bladder, and pelvic nodes is grossly incorrect and, due to the steep gradient of dosage rate, the errors may be large.

(2) *Calculations at Selected Points Based on Radiographic Localization:* One determines the nearest "rectal point" and "bladder point" by visualization on the antero-posterior and lateral films with sodium iodide in the bulb of a Foley catheter and barium on the anterior rectal wall. A number of other illustrative pelvic points are also chosen. Using the tables for linear sources, one then determines the dosage at the various points. The signifi-

cance of such "bladder and rectal doses" has been discussed.

(3) *Three-Dimensional Reconstruction Technics:* Exact three-dimensional reconstruction technics will give accurate data for isodose surfaces or points which are determined in reference to the applicators (6). Such systems do not solve the difficulty of the anatomical localization of the whole base of the bladder or a long strip of the anterior rectal wall.

We have used, in a number of applications, a technic slightly modified from that of Spiers (9), using sodium iodide in the bulb of the indwelling catheter and barium in the rectum (Fig. 5B). The data obtained for the nearest "bladder and rectal points," as determined from the radiograph, did not show any consistent relationship to the maximum doses obtained by direct measurements. Several points, and not only the "nearest point," ought to be studied for the rectum and bladder. These three-dimensional studies are time-consuming and impractical on a routine basis. The technic used for orthographic pelvimetry might yield more accurate data (3).

(4) *Direct Measurements:* With a probe containing at its tip either a scintillation crystal or a small ionization chamber and connected to a direct reading meter, measurements can be taken in the bladder and rectum (1, 4, 5) or along the pelvic wall, while the radium is *in situ*. The accuracy of the measurements depends entirely upon the positioning of the probe along the base of the bladder and the anterior rectal wall. In order to have a feeling of contact with the base of the bladder or the anterior rectal wall the probe must be light and long enough so that the housing of the photomultiplier in the scintillation case does not stand in the way (Fig. 1).

The anterior rectal wall is easily followed at the level of the rectovaginal septum and posterior fornix (behind vaginal radium) when the vagina is filled with packing or distended by the applicators. Distal to the isthmus, the position of the tip of the probe is no longer reliable, due

to the shift of the rectum to the left and the lack of rigidity of the wall at this level. (There is no constant structure except in case of a retroverted uterus and, in this instance, the readings are of importance at this high level.) As the rectal ulcerations are almost always behind the posterior fornix or the cervix, data above the level of the isthmus are not of practical significance.

The base of the bladder is more resilient and, in addition, the urethra diminishes the freedom of motion of the probe. A light probe, care, and experience are necessary to keep contact with the base of the bladder without depressing it. Even so, the same accuracy cannot be obtained as for the anterior rectal wall. A slight tilt of the probe and moderate pressure change the readings appreciably. An indirect proof of the clinical reliability and usefulness of the data, however, is furnished by the excellent correlation of the locations so obtained and intensity of "hot spots" with the position of the radium sources on the radiographs.

The probe is graduated in centimeters, and the physicist records the readings as the operator calls the depth of the insertion as he introduces it. In that fashion, doses are determined for the whole length of the base of the bladder and the anterior rectal wall. For the first insertions, the tip of the probe was shifted sideways, as it is desirable to know the dosage over the whole area. It was felt, however, that the location of the tip was too uncertain to justify reliance on data thus obtained.

The readings are taken in the lithotomy position and are significant only if there is no change during treatment time in the position of the base of the bladder and the anterior rectal wall. Due to the tight filling of the vagina by colpostat and packing, the rectovaginal septum is rigidly taut and no motion is possible. Also the tight packing and the forced supine position of the patient due to the protruding handles allow little motion; furthermore, the attachment of the base of the bladder to the anterior vaginal wall keeps the bladder in a constant relation to the vaginal radium.

Measurements cannot be taken with the patient on the back in bed, because of the impossibility of having the assurance that the tip of the probe is in contact with the base of the bladder or the anterior rectal wall. However, to spot-check the immobilization of the radium system, radiographs were taken every day (seventy-two hours insertion time), and no visible difference was found in relationship to the bony pelvis. The physical accuracy of the instrument is well within 10 per cent. The possibilities of added error from differences in positioning of the probe by various operators are minimized by experience. Comparative measurements in the same case by different persons have proved to be in close agreement. The direct measurements in conjunction with radiographic study have been an excellent guide to treatment and undoubtedly will minimize the complications in the bladder and rectum.

RADIUM TECHNIC AND DOSIMETRIC PROCEDURE

The radium applicators and the principles of the technic have been described elsewhere (1). The operating room technic is briefly outlined in the following paragraphs.

Spinal anesthesia is used if a tandem is to be employed. The loaded tandem is inserted and dummy plastic colpostats with handles are placed in each fornix. Readings are then taken in the bladder and rectum. Since the dummy plastic ovoids, although pushed up tightly by the handles, are not identical with the full packing, readings are not accurately representative of the contribution of the tandem alone. However, the readings together with radiographic information are of practical use in the choice of loading of the tandem in subsequent applications.

The loaded ovoids are then placed in position and readings are taken in anterior and posterior fornices and rectum. If the rectal readings are too high, packing is used between colpostat and rectovaginal septum; otherwise, packing is done in front of the cervix, to prevent slipping of the

uterine tandem, and around the handles, to prevent rotation of the colpostat. The packing is made as tight as possible to displace the whole radium system upward and posteriorly.

Final readings are made first in the bladder. The readings on the galvanometer increase up to maximum and then decrease. The probe is then withdrawn gently, keeping contact with the bladder wall, and readings are again taken. If the readings on entrance and withdrawal are in close agreement, one is assured that the tip of the probe has followed the wall. If there is a discrepancy between the two readings, the second readings are used, as it is easier to follow the bladder wall without applying pressure upon withdrawal of the probe.

The readings in the rectum are done in the same way as those in the bladder, skirting the anterior rectal wall and avoiding pressure. If the readings are excessive in spite of packing between colpostats and the rectovaginal septum, either tandem or colpostat or both are removed. If the readings are high, the radium is left until radiographs are available for a final decision. As soon as possible after the application, localization radiographs are taken. Sodium iodide is injected in the bulb of the Foley catheter and a clamp clipped to it at the urethral meatus. Barium paste is smeared on the anterior rectal wall (and at times barium has been injected into the rectosigmoid through a catheter). A small metal ring is fastened to the anus with Scotch tape. Two anteroposterior exposures are made on the same film, and a lateral view is taken (Fig. 5).

If the readings are within tolerance (3,000 to 3,500 gamma roentgens), and the position of tandem and ovoid as shown on the radiographs is satisfactory, the radium is left for seventy-two hours. If the application is unsatisfactory, the radium is removed and tandem and/or colpostat changed. The measurement of the uterine cavity with a probe and the fitting of the vagina by means of dummy colpostats in the clinic, before the radium application, reduce such

occurrences to a minimum. If the readings are high, the treatment time may be cut to less than seventy-two hours or the loading modified in the next insertion.

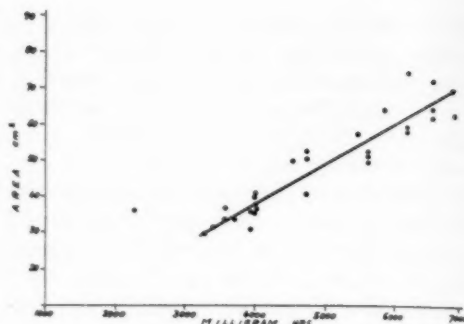
From the films a three-dimensional reconstruction can be done on a dose finder (1) and doses can be calculated at any anatomic point as necessary (Fig. 1).

On each application, based on the films, the lateral throw-off in the plane defined by the center of the vaginal radium and a point 2 cm. above the lower end of the tandem is studied. In this plane a 3,500 r isodose curve is drawn and the dose every half centimeter lateral to the tandem is noted (Fig. 3). These data will be the guide for the planning of the complementary external irradiation.

The loading of the system for the first application is determined by the length of the tandem, and the size and separation of the colpostats, as described elsewhere. Loading for the second application depends on the readings and radiographs of the previous insertions. The total dose delivered to the bladder is kept below 7,500 gamma roentgens and to the rectum below 7,000 gamma roentgens. If external irradiation has been given to the mid-line as a pre-radium treatment, the total dose—x-ray plus gamma ray—is kept below 7,000 r for the bladder and 6,500 r for the rectum. The length of the strip where the dose is above 4,000 r is also considered in the determination of the maximum dose. The number of milligram hours varies from 2,500 to 7,000 per insertion and the total for a complete treatment from 5,000 to 12,000 milligram hours.

MEASUREMENTS AT THE TIME OF EXTRAPERITONEAL LYMPHADENECTOMY WITH RADIUM IN SITU

In a series of Stage I and early Stage II cervical carcinomas, which were being treated by a combination of radium therapy and extraperitoneal lymphadenectomy, a number of cases were chosen for operation at the end of radium treatment. The selection was made in order to have a variety of radium distributions—ovoids



Graph 1. The graph shows a linear increase of the area within 3,500 gamma roentgen isodose curves (it would be the same function if one had chosen the 1,500 or 1,000 gamma roentgen curves). Three factors contribute to this increase: (a) increase in milligram/hours; (b) larger diameter and greater separation of the ovoids; (c) longer tandems.

alone, tandem alone, whole radium system—in vaginas of different sizes and degrees of elasticity. When the pelvic wall is exposed and node groups are identified, the tip of the probe is placed on the nodes and readings are taken. Measurements are also made at other points of the pelvis: next to the fornix at the upper aspect of the ovoid, straight lateral on the pelvic wall, upper aspect of obturator foramen, crossing of ureter and uterine artery. The so-called "ureteral node" cannot be identified as a rule.

DISCUSSION

(1) In 77 of 145 insertions, or about 50 per cent, the tandem and a pair of ovoids were introduced at the same time. The large number of fractionated treatments indicates the usefulness of a set of uterine tandems that can be used independently from the colpostat.

(2) With a few exceptions, readings agree with the geometry of the radium sources in relationship to bladder and rectum. This means that even if the figures are not absolutely accurate, the procedure is basically reliable. One can predict the existence and probable location of "hot spots" from the films and have it confirmed by readings or, *vice versa*, predict the geometry from the readings and have it confirmed on the films.

(6) Measurements taken with tandem.

then with tandem, colpostat, and packing, have repeatedly demonstrated that the tandem contributes most to the bladder dose, more so in case of a long tandem and antelexion. The area of maximum dosage is distal to the bladder neck, at the junction of the base of the bladder with

(7) In many cases the readings for the tandem alone were higher or close to readings for the tandem plus ovoids and packing. The points of maximum doses with the tandem alone were also displaced distally. This emphasizes the influence of packing not only between colpostat and

Number of Sources Tandem Only	B L A D D E R				R E C T U M			
	#	Maximum	** Distance	*** Range	#	Maximum	** Distance	*** Range
3 Sources (15 - 10 - 10)	32	2903	78	2-6	32	2553	74	3-2
2 Sources (15 - 10)	44	2157	72	1-7	46	2669	73	2-6
1 Source (10)	10	1776	72	1-5	10	2044	78	2-4
Angulation *								
0 - 59	31	2811	78	2-6	33	2538	77	3-2
60 - 89	25	2171	73	1-6	26	2065	72	2-08
90 and over	30	2139	71	1-5	29	3016	7-2	3-0

* Between Axis of Ovoid and Axis of Tandem

*** Length of strip over 2,000 γ roentgens

** Distance from urethral meatus or anal margin

TABLE II: The figures are for a standard seventy-two hours. Rectal doses (maximum dose and length of strip above 2,000 gamma roentgens) are relatively unaffected by the length of the tandem and degree of flexion. In contradistinction, bladder doses (maximum dose and length of strip above 2,000 gamma roentgens) are decidedly higher for longer tandems and in the presence of antelexion (0-59°). This confirms the conclusion drawn from the bladder readings with tandem alone before the vaginal radium is inserted.

the posterior wall. This is to be expected from the geometry of the sources. Table II shows the increase in the maximum bladder dose and the area receiving over 2,000 gamma roentgens for longer tandems and greater antelexion. The rectal dose is less affected by loading and position of the tandem. Even marked retroflexion does not produce high doses, provided uterine and vaginal sources are not too crowded (Fig. 6). These conclusions are valid only for the applicators we use. The respective contributions from tandem and colpostat might be different for applicators of other types.

rectovaginal septum but in the whole vagina. Such packing will displace the whole radium system upward and posteriorly, thus reducing by distance the dose to the bladder and rectum. The handles of the colpostat are a major factor in this displacement. In addition, broad ligaments and pelvic nodes are better irradiated. The paracervical tissues and uterosacral ligaments move with the uterus, since they are fastened to it and are little affected by this displacement. If the colpostat is used alone, bladder readings are maximum at the level and immediately distal to the bladder neck. With tandem plus

Case	Insertion	Load	B L A D D E R			R E C T U M				REMARKS	LYMPHADENECTOMY READINGS
			Base of Bulb	Point of Maximum Dose	Tandem alone (before insertion of ovoids)	Total High	Length of strip above 2,000 r (in cm.)	Level of Colpostat	Point of Maximum Dose		
#8537	I	10 20 30 40 50 60 70 80 90 100 110 120 130 140 150 160 170 180 190 200 210 220 230 240 250 260 270 280 290 300 310 320 330 340 350 360 370 380 390 400 410 420 430 440 450 460 470 480 490 500 510 520 530 540 550 560 570 580 590 600 610 620 630 640 650 660 670 680 690 700 710 720 730 740 750 760 770 780 790 800 810 820 830 840 850 860 870 880 890 900 910 920 930 940 950 960 970 980 990 1000 1010 1020 1030 1040 1050 1060 1070 1080 1090 1100 1110 1120 1130 1140 1150 1160 1170 1180 1190 1200 1210 1220 1230 1240 1250 1260 1270 1280 1290 1300 1310 1320 1330 1340 1350 1360 1370 1380 1390 1400 1410 1420 1430 1440 1450 1460 1470 1480 1490 1500 1510 1520 1530 1540 1550 1560 1570 1580 1590 1600 1610 1620 1630 1640 1650 1660 1670 1680 1690 1700 1710 1720 1730 1740 1750 1760 1770 1780 1790 1800 1810 1820 1830 1840 1850 1860 1870 1880 1890 1900 1910 1920 1930 1940 1950 1960 1970 1980 1990 2000 2010 2020 2030 2040 2050 2060 2070 2080 2090 2100 2110 2120 2130 2140 2150 2160 2170 2180 2190 2200 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common case in old patients with atrophy of the vaginal vault and of the uterus, which is generally in retrocession. In these odd insertions, direct measurements are of the greatest value in avoiding overdosages.

(10) A classical type of loading of tandem and colpostats has been used. Study of the shape of isodose curves in the plane passing through the paracervical triangle shows that in anteфлекed uteri, due to the short distance between paracervical tissues and vaginal radium sources, the paracervical tissues are better treated. This is another reason to believe that little advantage is to be gained by attempting to reduce the anteфlection of the uterus by a rigid single-piece applicator. In mid-positioned uteri the lateral throw-off at the level of the internal os of the cervical canal is mostly a function of length and loading of the tandem. In view of the relatively high contribution of the uterine tandem to the pelvic nodes, heavier loading of the tandem and lesser loading of the colpostat ought to be tried. This can be done safely with direct measurements in rectum and bladder.

(11) Intracavitary radiotherapy is glaringly inadequate (Fig. 3) without at least two sources in the uterine tandem and two vaginal cylinders. Otherwise, the volume of adequate irradiation is limited to a thin band of tissue surrounding the vault. In such cases external irradiation should be used to its full advantage.

CONCLUSION

(1) Direct measurements in bladder and rectum, calculations by a semi three-dimensional reconstruction technic of the 7,000 gamma roentgen isodose curve in the plane passing through the paracervical triangle, and the estimation of range of doses to pelvic nodes, offer a practical system of dosimetry to be used in the guidance of treatments. This individualized procedure of dosimetry is proving to be an important step in the understanding of the proper use of radium in varying anatomical situations.

(2) Individualization to fit the anatomical situation is essential. The use of a system employing independent and flexible applicators represents a great advantage of fitting the infinite variety of actual cases. Such applicators afford a thorough treatment of the primary lesion with an associated improved lateral throw-off of the dose even in many difficult cases. The optimum respective loading of tandem and colpostat has not yet been determined.

(3) A high position of the radium system and a wide separation of vaginal radium sources is advantageous in treating extension of the disease toward the pelvic wall.

(4) Points A and B are not representative of any structure or line of spread of the disease. Calculations at these points may be useful in the theory of a particular radium technic, as their ratio is an index of the lateral throw-off at the level of the internal os.

(5) In the past, the incidence and severity of reaction have not been correlated with accurately calculated or measured doses to the bladder and rectum. In this institution, it was decided to set temporarily maximum doses, arbitrarily, slightly higher than the accepted averages. Experience will show the necessity of further modification.

(6) External irradiation should be used to its fullest advantage when the distribution of the radium sources is not optimal.

M. D. Anderson Hospital
University of Texas
Houston, Texas

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SUMARIO

Mediciones Directas y Cálculos de los dosis en la Radioterapia del Carcinoma del Cuello Uterino

Ofrécese un método práctico de dosimetría para empleo en el carcinoma del cuello uterino, comprendiendo mediciones directas de la dosis en la vejiga y el recto, cálculos con una técnica semi-tri-dimensional de reconstrucción de la curva de isodosis de 7,000 roentgens gamma en el plano que atraviesa el triángulo paracervical, y cálculo aproximado de la escala de dosis aplicados a los ganglios pelvianos.

La individualización adaptada a los sitios anatómicos es indispensable. El uso de un sistema que utilice aplicadores independientes y flexibles representa una gran ventaja para acomodarse a la inmensa variedad de casos que se encuentran en la práctica. Esos aplicadores proporcionan un tratamiento adecuado de la lesión primaria junto con una emisión lateral mejor de la dosis, aun en muchos casos difíciles. No se ha determinado aun la óptima carga respectiva del tandem y del colpóstato.

Una posición elevada de la instalación de

radio y una amplia separación entre los focos vaginales de radio resultan ventajosas al tratar la difusión de la enfermedad hacia la pared pelviana.

Los puntos A y B no representan ningún tejido ni línea de propagación de la enfermedad. Los cálculos ejecutados en dichos puntos pueden ser útiles al aplicar alguna técnica dada de curieterapia, pues la razón entre ellos constituye un índice de la emisión lateral al nivel del orificio uterino interno.

En el pasado, no se han correlacionado la incidencia e intensidad de la reacción con dosis calculadas o medidas exactamente aplicadas a la vejiga y al recto. En el establecimiento de los AA., se acordó fijar temporalmente dosis máximas, arbitrariamente algo mayores que los promedios aceptados.

Hay que usar en toda su plenitud la irradiación externa siempre que no sea óptima la distribución de los focos de radio.

DISCUSSION

Kenneth E. Corrigan, Ph.D. (Detroit, Mich.): So much of the content of the paper by Dr. Fletcher and his group is purely clinical that I found it necessary to call upon Dr. James Cook of our own department and my great mentor of former years, Dr. Edwin C. Ernst, who introduced me to the clinical application of physical radium measurements just twenty-three years ago. Thus, at least I have arranged to disavow any personal responsibility for the clinical aspects of this discussion.

From the purely physical point of view, it appears that the authors have collected almost all

that was good in the established knowledge of the subject and have made several very nice advances. Their illustrations and descriptive matter again demonstrate a fact that can never be over-emphasized, that the human animal absolutely is not a die-cast product, but that each and every one is an individual problem. Failure to respect this concept has led many mechanized routines of both therapy and diagnosis to the intellectual graveyard. Success in clinical radium therapy still depends on the skill of an individual operator applying his knowledge and experience to the unique problems of an individual patient.

The most skillful operators, however, need two physical aids, first a method of predicting with reasonable accuracy the depth and volume dosage which will result from their technic; second, a means of checking their procedure *in situ*, before it is too late.

Probably one of the most important aspects of the entire development is a factor which the essayists have not stressed. This is the teaching aspect, including the vital self-teaching, which must go forward after a trained man has left the

parent institution and begins to encounter problems which are never quite like those he saw in training. The instrumentation developed by Dr. Fletcher and his associates offers both a valuable new research procedure for large institutions and a reliable procedure which may be used by those who have no clinician with a lifetime of experience nor a complete physics staff to fall back upon. Thus, they offer both a technic for advancing knowledge and a means of avoiding disaster. They are to be congratulated.



Transport of Radium Sulfate from the Lung and Its Elimination from the Human Body Following Single Accidental Exposures¹

L. D. MARINELLI, M.A., W. P. NORRIS, Ph.D., P. F. GUSTAFSON, B.S., and T. W. SPECKMAN, B.S.

IN THE PRESENCE of insoluble radioactive dust, it is not always possible to determine whether the permissible level in air should be governed by the radiation delivered to the lung and air passages or by the radiation delivered to the critical organ where ultimately most of the radioelement, mobilized from the lung but not excreted by the body, will be deposited. This perplexing situation is created not so much by lack of knowledge of the fraction deposited in the various parts of the respiratory tract (1-3) as by the scarcity of information on the rate of elimination of the particulate matter by the human lung. This statement applies not only to the recently discovered artificial radioelements but extends also to radium, which as early as 1926 was shown by Reitter and Martland (4) to gain access to the skeleton by way of the lungs.

In order to gather information on the subject, six individuals exposed to radium sulfate dust as a consequence of two industrial accidents were selected for study. Five persons (R., K., Ch., Ca., and S.) from the first accident (5) have been studied for a period of a year, through the collaboration of Dr. Eugene L. Saenger of the Cincinnati General Hospital; the sixth, technician G. from our laboratory, has been followed more closely for 250 days and will be under observation to the limit of our resources in sensitivity. In both instances the inhalation lasted for only a few minutes following the rupture of 50-mg. radium capsules containing approximately equal parts of RaSO_4 and BaSO_4 .

This study is based on the following observations: (a) exhalation rate of radon,

(b) measurements of gamma-ray activity from the whole body, (c) measurement of gamma-ray activity from the thorax, and (d) measurement of radium in the excreta. It has been possible to estimate from *a* and *b* the total-body burden according to accepted practice, and to gain by means of procedure *c* some information as to the localization of the RaSO_4 . Owing to difficulties of a practical nature, a complete excretion study was feasible only in the case of our technician; only scattered data are available for the others.

THE BODY BURDEN

The quantity of radium in the body which produces radon at the rate exhaled by the host can be computed by the expression:

$$1 \mu\text{g. Ra} \equiv 2.1 \mu\text{c. Rn per second}$$

This fraction does not contribute to the measured gamma-ray activity and it is, therefore, added to the latter in the estimate of the total radium burden.

After appropriate trapping of water, and through a continuous process of adsorption, all the radon contained in the air exhaled by a patient in ten- to twenty-minute periods was collected on charcoal. The radioactive gas was then transferred into suitable ionization chambers connected to an electrometer, and the calibration was performed by comparison with the ionization produced by known fractions of Rn liberated by standardized radium solutions. By such large sampling the sensitivity of detection may be increased considerably over the more conventional technic which utilizes only one

¹ From the Division of Biological and Medical Research, Argonne National Laboratory, Lemont, Ill. Presented at the Thirty-eighth Annual Meeting of the Radiological Society of North America, Cincinnati, Ohio, Dec. 7-12, 1952.

or two liters of air, and, for equal exhalation rates, the precision of the measurement is likewise improved.²

The gamma-ray activity of the whole body was measured, whenever possible, by a modification of the basic method originated by R. D. Evans (6) in his in-

long), attached to a 5819 photomultiplier provided with a linear amplifier and single channel pulse analyzer with variable band width.³

Experiments were performed to utilize the spectrometric potentialities of this counter in order (a) to increase the ratio

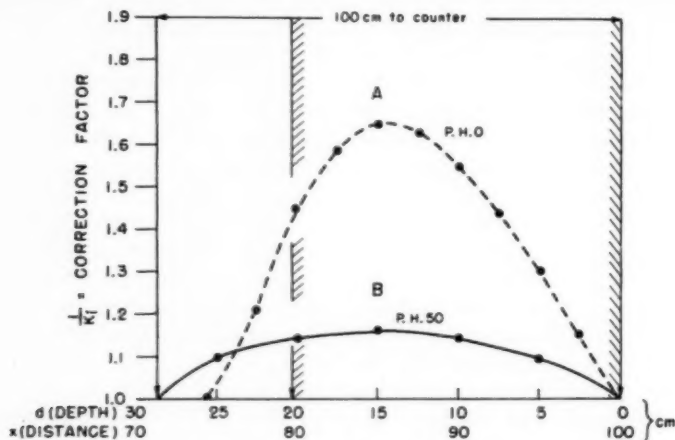


Fig. 1. Variation of the scattering correction factor K_1 with depth of Ra source in a Presdwood phantom of thickness $t = 20$ cm. and 30×30 cm. portal area. Curve A: Band width 30-370 kev. Curve B: Band width above 370 kev.

The distance, x , between the detector crystal and the back of the phantom is kept fixed at 1 meter; depth, d , is measured from the distal surface of the phantom.

vestigations on chronic radium poisoning. Whenever the Ra content of an individual was found too low to yield significant results by this method, the estimate was based on direct comparison with the more "active" individuals of the group, properly measured by the basic method, and rigidly seated in a "Standard" chair under reproducible conditions. Although the latter procedure is open to objections, on the ground that it is valid only when the patterns of Ra deposition in the body are identical, it was felt that errors were minimized by restricting the comparison to individuals who were exposed to Ra at the same time. An increase in sensitivity of a factor of about ten could be obtained with reasonable accuracy. The detecting instrument consisted of a NaI crystal (1.5 inches in diameter and 2.5 inches

of the patient signal to the background noise accruing mainly from natural radioactivity in the surroundings and (b) to ascertain whether the estimates of radium content in any single individual would prove independent of the pulse size band selected for measurement. It was found that the signal (*circa* 500 counts per minute per microgram of Ra at 1 meter) to background noise ratio could be substantially improved by operating in a room lined with 1/8 to 1/4 inch of lead and by registering all pulses generated by electrons of energy between 30 to 370 kev.

Studies of the response of the counter to the presence of Ra embedded at different depths in either Presdwood or water phantoms indicated that, on account of

³ The authors are indebted to Dr. C. E. Miller and Mr. R. E. Rowland, of the Radiological Physics Division, for the design and construction of this remarkably stable instrument.

² Details of the technic will be published elsewhere.

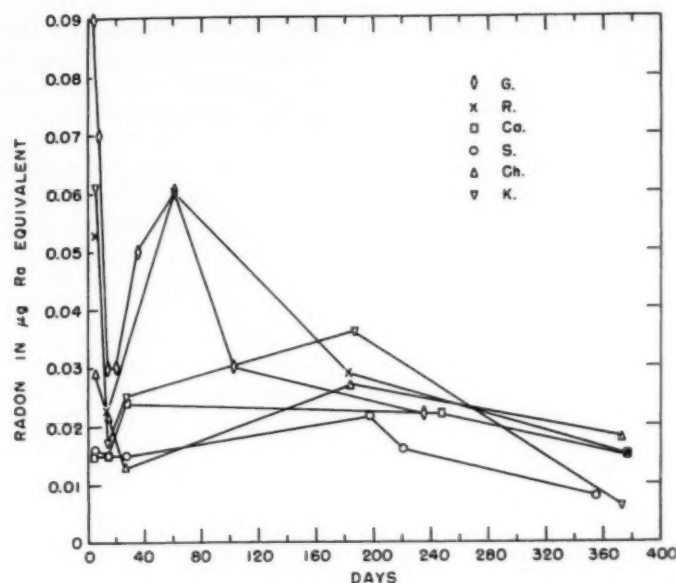


Fig. 2. Exhalation rates of radon, in μg . of Ra equivalent, plotted as a function of time after accidental exposure.

gamma-ray scattering, the counting rate depended in a complex manner on the depth of the source, on the thickness of the phantom, and on the pulse height band of the analyzer. When the distance from the back of the phantom to the counter was kept fixed at 1 meter, the counting depth dose curve, per microgram of Ra, could be expressed as

$$K_1 N_4 x^{-2} e^{-\mu d}$$

where

- μ = coefficient of absorption per centimeter of phantom (broad beam)
- d = depth of source in phantom in centimeters
- x = source to counter distance in meters
- N_4 = net counting rate due to 1 μg . at 1 meter in air
- K_1 = a scattering correction factor which depends on d and on the pulse height band selected for measurement

The variation of K_1 with d for two pulse height widths is illustrated in Figure 1.

Following Evans's analysis, the Ra burden in any individual can be written as:

$$\mu\text{g.} = K(1 - t)(N_1 N_2 / N_4^2 e^{-\mu d})^{1/2}$$

where

- t = ratio of the average thickness of patient to the distance of the counter to the distal surface of the patient
- N_1 = net reading of patient facing counter when placed on arc of a circle 1 meter in radius, the center of which is at the counter
- N_2 = same as N_1 but with patient facing away from counter

The factor K is calculated by the expression $K = (K_1 K_1')^{1/2}$, where K_1 and K_1' are the scattering correction factors corresponding to depths d and $(t-d)$ respectively; they can be read off Figure 1 for the particular phantom thickness illustrated. The variation of K with depth of the source is rather small, especially if the pulse height band above 370 kev. is used. This, however, is not always possible if the gamma activity is low, since the ratio of the signal to background noise is then considerably smaller. It is preferable in these instances to risk a greater, but definitely limited, uncertainty in K in order to gain adequate statistical accuracy in determining N_1 and N_2 .

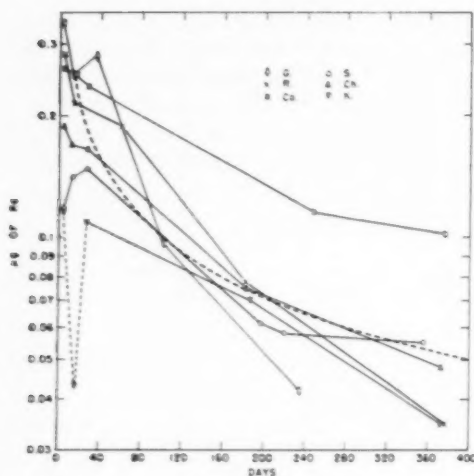


Fig. 3. Total Ra burden in the body (log scale) estimated from both Rn and gamma-ray activity measurements. Dashed curve: theoretical fractional retention of soluble salts, equation (2)

On the assumption of an average depth $d \approx 5$ cm. we have calculated: $K = 0.7$ as the scattering factor for pulse height band 30–370 kev. and $K = 0.93$ for pulse sizes above 370 kev. Confidence in this procedure has been established by measurements on cases of chronic Ra poisoning, in test subjects to whom known amounts of Na^{24} were administered orally, and in a balance study performed with one of our cases (*vide infra*).⁴

The exhalation rates of Rn, expressed in equivalent micrograms of Ra, are plotted in Figure 2. It will be noticed that all but 2 of the cases show a sharp decrease within 15 days of the exposure, followed by an increase, and later by a more moderate decrease. It is realized at this time that the exhalation of Rn should have been followed

more closely during the 15- to 180-day interval as exemplified by the curve obtained from our technician (G.). Although there exists a possibility that, in the Cincinnati cases, the initial decrease in Rn exhalation might reflect in part the decrease in Rn content of the laboratory air in the first two weeks following the accident, there is much more reason to suspect that this decrease is due instead to the excretion of radium dust initially swallowed and dissolved in the gastrointestinal tract. This view is supported by the fact that similar behavior was exhibited by Rn exhaled by our technician (who was removed from any Rn contamination immediately following the second accident) and in particular by his excretion pattern (*vide infra*).

THE TOTAL-BODY BURDEN

The sum of the fractions yielded by Rn and gamma-ray activity measurements is shown in Figure 3 as a function of time after exposure. Since it was not feasible to proceed with the measurements on the first day of the accidents, it is impossible to compare directly the retentions with those investigated by Norris and Kiseleski (7), Hurst (8), and Norris *et al.* (9) in experimental animals and in man following injection of RaCl_2 . It is possible, however, to compare the slope of the curves. It will be recalled that these investigators found that the rate of excretions dq/dt could be related to the injected amount, q_0 , by an expression of the following type

$$dq/dt = -Aq_0(t+1)^{-b} \quad (1)$$

where A and b are constants. Upon integration, the retention, q , becomes

$$q = q_0 \left\{ 1 + \frac{A}{1-b} [1 - (t+1)^{1-b}] \right\} \quad (2)$$

If in the last equation values of the constants are assumed in fair accord with the data on RaCl_2 injected in animals and man ($A = 0.50$, $b = 1.50$), the dotted line in Figure 3 is obtained. By inspection, it can be ascertained that the slopes are roughly similar but that in some

⁴ In a group of 6 Ra cases, the maximum discrepancy obtained by the use of the two pulse heights was ± 11 per cent for any one individual and less than 3 per cent on the averages for the groups.

In the experimental group given Na^{24} , all measurements yielded consistent results within 10 per cent of the actual amount given, although the weights of the volunteers ranged from 96 to 176 pounds. Moreover, although measurements were made from one minute to thirty-six hours following ingestion, the computed amount remained constant despite the considerable diffusion of the radioelement within that time. A more detailed evaluation of the method will be presented elsewhere.

cases the retention of inhaled RaSO_4 will be less than that expected from injection of soluble Ra salts. We shall have an opportunity to return to this subject later in this paper.

Of practical interest are the ratios of Rn to total Ra found in this group. They are shown in Table I for those cases in which measurements of total gamma-ray activity by the absolute method were possible and hence more reliable. It should be noted that they are lower than the values re-

ported in cases of chronic Ra poisoning many years after the date of administration (6, 9). Therefore, shortly after an inhalation accident, the burden is likely to be underestimated severalfold if the current practice of assuming the chronic partition coefficient of 0.5 for Rn is adopted, but the error would be smaller if the exposure had lasted for several years. Except for venturing that the ratio of Rn to Ra is low because some of the Ra is retained in the non-emanating form of RaSO_4 , we are un-

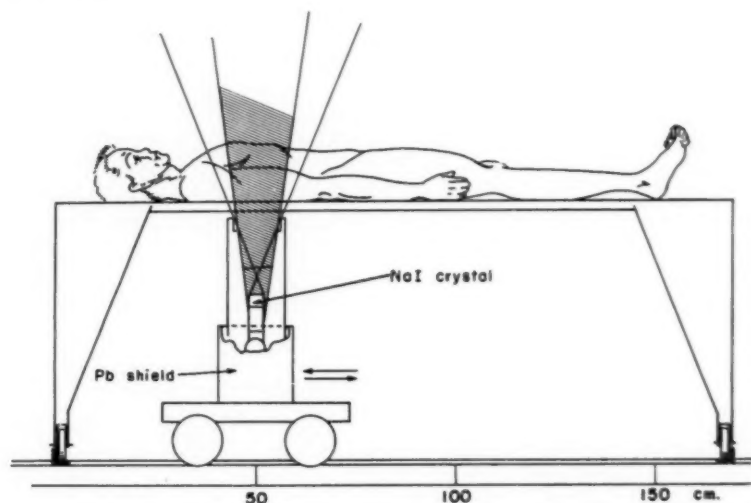


Fig. 4. Arrangement for the investigation of localized sources of gamma-ray activity (scanning measurements).

TABLE I: MEASUREMENT PATTERN OF CASES R., CA., AND G.*

Days (1)	Name (2)	Rn (3)	Body γ-Ray (4)	Total Radium (5)	Rn/Total Ra (6)	Calculated Extra Skele- tal Ra (7)	γ-Lung (8)	Ratio (9)
61	R.	0.060	0.128	0.188	0.32	0.102	0.045	2.26
182	R.	0.029	0.049	0.078	0.37	0.037	0.023	1.61
27	Ca.	0.024	0.211	0.235	0.10	0.201	0.113	1.78
247	Ca.	0.022	0.094	0.116	0.19	0.085	0.036	2.36
376	Ca.	0.015	0.087	0.102	0.15	0.081	0.027	3.00
3	G.	0.09	0.248	0.338	0.27	0.210	0.245	0.86
13	G.	0.03	0.222	0.252	0.12	0.209	0.194	1.08
35†	G.	0.05	0.232	0.282	0.18	0.211	0.102	2.07
35‡	G.	0.05	...	0.200	0.25	0.111	0.102	1.09
102	G.	0.03	0.067	0.097	0.31	0.054	0.029	1.86
235	G.	0.022	0.02	0.042	0.52	0.011	0.010	1.10

* Quantities in columns 3, 4, and 8 were measured directly. Column 7 was calculated as difference between values of Column 5 and skeletal radium. The latter was assumed to be given by the Rn values (Column 3) divided by the partition coefficient $\text{Rn/Ra total} = 0.7$ found by Norris *et al.* (9) as an average in cases of chronic Ra poisoning. In Column 9 are the ratios of the values of Column 7 to Column 8 (see text).

† Measurements based on Rn and gamma-ray activity.

‡ Estimate based on measurements of burden at three days less intervening excretion.

able to explain its relative constancy in the first two cases shown in Table I. Its tendency to reach higher values in the third case, as the time interval between accident and observation increases, could be attributed to redistribution and ultimate deposition in bone. Although par-

looked at a circular section of the chest, 15 cm. in diameter at the height of 10 cm. above the table. Travel of the table and counter along two mutually perpendicular axes allowed exploration of any region of the body. Typical traces of the activity detected along the axis of the body are

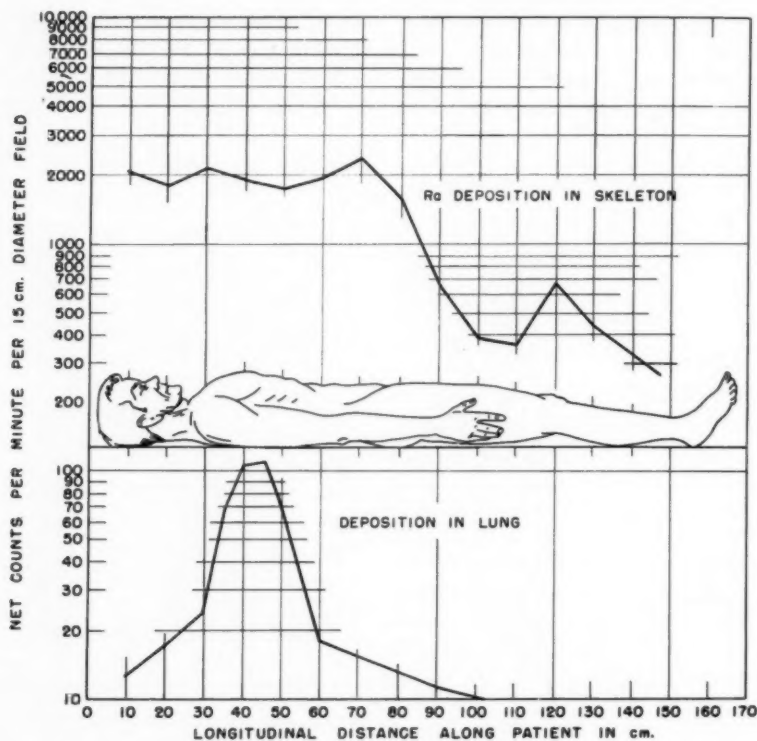


Fig. 5. Typical gamma-ray scanning curves. Above: Ra deposition in the skeleton 25 years after injection of RaCl_2 . Below: Deposition in the lung in case R. 61 days following accidental inhalation of RaSO_4 .

ticle size of the salt may play a role in the data presented here, we are in no position to evaluate its importance since, due to the accidental nature of the exposure, no special study of this type was possible at the moment in which inhalation took place.

THE LUNG BURDEN

The localization of Ra in the lung was studied by scanning the thorax with a scintillation counter according to the scheme illustrated in Figure 4. The NaI crystal, provided with a lead collimator,

shown in Figure 5; they illustrate the different patterns provided by skeletal and pulmonary deposition.

The most complete set of readings obtained in a single individual of our group (G.) is shown in part in Figure 6. It will be noticed that transverse scanning yields curves wholly comparable with those obtained by longitudinal scanning and that in this case the Ra must have been concentrated originally in a rather small volume (~ 300 c.c.) centered at the level of 4th or 5th thoracic vertebra. The latter state-

ment is self-evident when the half-width⁶ of the curve at 7 days after exposure is compared with the half-width obtained by moving a point source at mid-point of a 20 × 30 × 30-cm. phantom of Presdwood. Because of the long counting times required to yield estimates of reasonable precision,

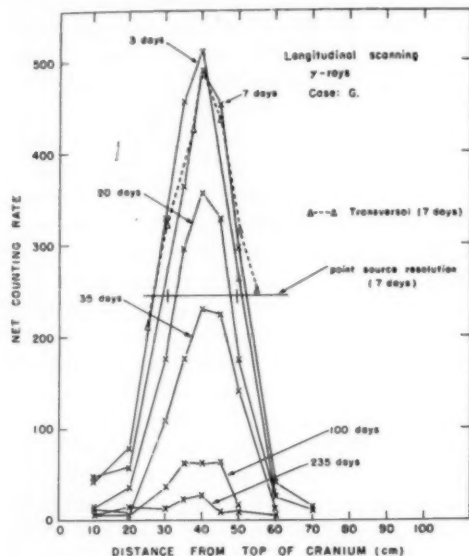


Fig. 6. Gamma-ray scanning curves along longitudinal axis of subject G.

not all cases were scanned to the same extent. Instead, a few regions around the field of maximum activity were surveyed for periods as long as a year. To account for changes in counter sensitivity, the gamma-ray activity was compared with that of a known amount of Ra located as a point source on the collimator axis in a phantom 20 cm. thick at a height equal to half the thickness of the person's chest. This procedure was deemed justified, since equality in readings obtained with the patient in the prone and supine positions indicated that the deposits were roughly symmetrical with respect to the median anteroposterior plane. By integration of the area under the *in vivo* scanning curves,⁶

⁶ Width of the curve at a height equal to one-half the maximum height.

⁷ More correctly volumes under curved surfaces, approximately conical in shape.

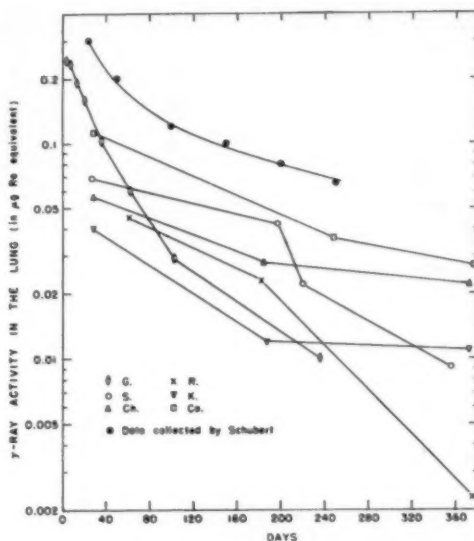


Fig. 7. The time variation of the total gamma-ray activity in the lung, expressed in $\mu\text{g.}$ of Ra equivalent. Data collected by Schubert (11).

and by comparison with areas under analogous curves obtained by scanning the Ra source, it is possible to arrive at fair estimates of the total gamma-ray activities in the lungs in terms of a Ra source in equilibrium with its decay products. These are shown in Figure 7, plotted on a semilogarithmic scale as a function of time.

Although these data do not carry *per se* unambiguous meaning on Ra metabolism—since they could be influenced by an indeterminate change in the Rn-emanating fraction of the lung deposit—they are, nevertheless, of direct significance in the field of radiation protection.⁷

It will be noted that the decrease is not always exponential and that the half-lives vary from 32 to 140 days within 6 months after exposure. The average is 118 days with a root mean square deviation of ± 25 per cent.

It should be noted that, although for two individuals the decrease in lung activity is distressingly small from about 6 months to a year, no account has been taken of the presence of extrapulmonary

⁷ This statement becomes obvious when one considers that the disintegrations of Ra in the body, not followed by the exhalation of Rn, are, energetically speaking, about six times as effective as those that are.

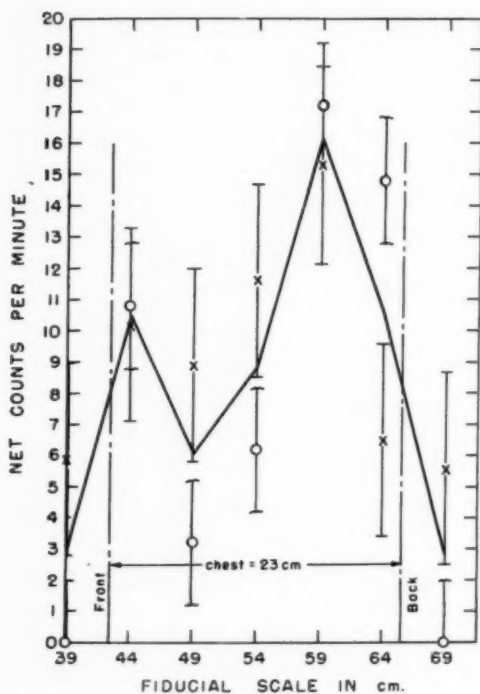


Fig. 8. Anteroposterior scanning curve of subject G., x at 264 days, O 241 days. Curve represents the average. Note rather large experimental error.

Ra within the field of view of the counter. A suitable correction for this could not be made in general because of the low activities involved. An attempt was made for the case of G. by scanning several times at a single level with the subject lying on his side and with his arms out of the field of the counter. Although the evidence (Fig. 8) is not complete, because the scanning was not repeated at various levels of the thoracic skeleton, it indicates, nevertheless, a certain correlation between counting rate and bone mass. Such correction could lower the values of Figure 7 by as much as one-third, beyond the time interval of 6 months. If this be true, the biological half-life of 120 days on the average would extend to as long as a year after inhalation.⁸

These findings, therefore, are reassuring from the standpoint of lung transport but

⁸ This half-life is similar to that found by the Rochester group in the lungs of dog exposed to uranium oxide (10) and consistent with the data gathered by Schubert (11).

point rather critically to the need of establishing the concentration of inhaled deposits with a precision higher than that attainable with our scanning methods.

THE EXCRETION OF RADIUM

Circumstances of practical nature precluded significant measurements of excreta from the Cincinnati cases, but adequate data were obtained for the case of our technician (G.) through the collaboration of the bioassay laboratory of the Health Services Division.⁹ Both feces and urine samples were frequently assayed for radium content by the technic described by Russell, Lesko, and Schubert (12). Although complete 24-hour collections were rarely possible, the radium content in the latter was estimated on the basis of a urinary daily output of 1,250 c.c. and a dry fecal sample of 30 gm. per day, in accordance with accepted physiological data (13, 14). The urinary excretion represented 2 to 8 per cent of the total. By integration of the total excretion curve for suitable intervals of time, and by the subtraction of the values thus obtained from the total-body burden measured at 3 days, it was possible to compute the retention at later times and to compare it with the total-body content as estimated by means of Rn and gamma-ray measurements. The results of the comparison are shown in Figure 9, where it can be seen that, except for the values at 35 days, the agreement between the two estimates is entirely satisfactory.¹⁰

For the purpose of discussion, the rate of total excretion is plotted in Figure 10 as percentage of body burden; it is compared with the values reported by Aub *et al.* (15) on a human case following inhalation of RaCl_2 dust. It will be noticed that, although in the latter instance excretion can be expressed satisfactorily as

⁹ We are indebted to Dr. L. S. Myers for these valuable data.

¹⁰ The agreement at 35 days could be substantially improved if the assumption were made that this person consumed during the summer months less food than in the succeeding winter and hence that the dry fecal sample was 20 instead of 30 grams.

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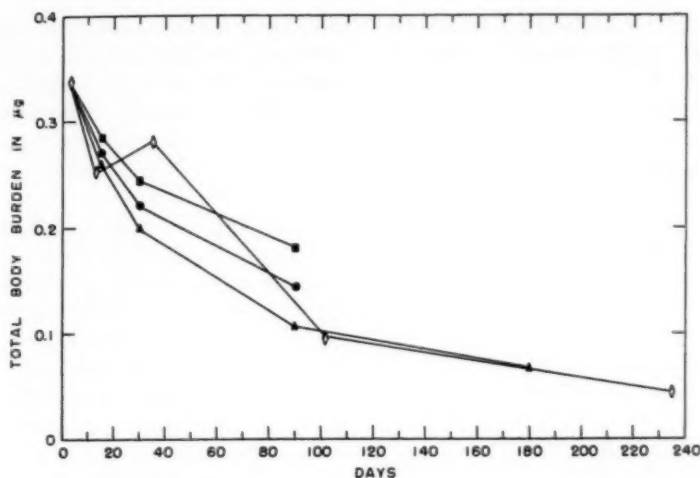


Fig. 9. Subject G. Comparison between estimates of body burden. \diamond = values obtained by direct measurements of Rn and gamma-ray activity. \bullet , \bullet , and \blacktriangle = values obtained by subtracting from the burden at 3 days the integrated total excretion. The latter was computed on the basis of 20, 25, and 30 gm. of dry feces per day and 1,250 c.c. daily urinary output. Date of accident June 13, 1952.

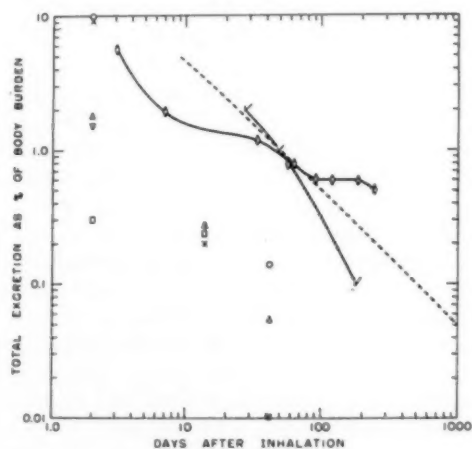


Fig. 10. The daily excretion expressed as per cent of body burden. \diamond Case G (RaSO_4 inhalation). ∇ Case RL. (RaCl_2 inhalation) (Ref. 15). The broken line represents the theoretical value based on a power function of time, equation (1). Other points: scattered data from Cincinnati cases according to key of Figure 2.

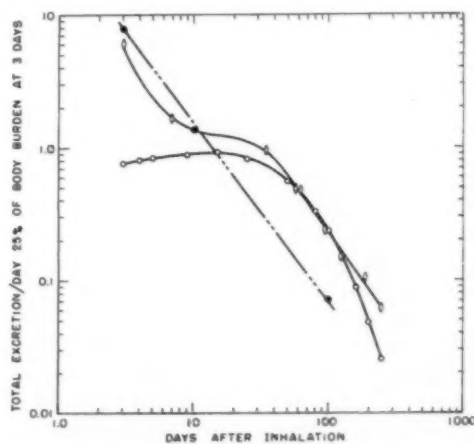


Fig. 11. Daily excretion expressed as per cent of Ra content 3 days following exposure. \diamond Case G. \bullet Average data of Hurst (8) and Norris (9) on dogs injected with RaCl_2 . \circ the theoretical excretion curve, equation (3).

an inverse power function of time, this cannot be done following RaSO_4 inhalation. Our excretion data are also shown in Figure 11, where they are plotted as percentage of body burden at 3 days in order to compare them with similarly plotted results of Hurst (8) and Norris *et al.* (9) on

dogs injected with RaCl_2 . The fair agreement in slope exhibited by the two curves for the first few days suggests that the initial excretion phase of G. could be ascribed to elimination of RaSO_4 ingested¹¹

¹¹ Ingested either directly or as a result of swallowing the dust mobilized from the trachea and bronchial tree by ciliary action.

and subsequently solubilized by the gastrointestinal tract. This view is consistent with known solubility of RaSO_4 ; it finds support, also, from (a) the fact that the Rn exhaled—presumably set free from the dissolved Ra in the gut—has been observed to decrease rapidly during this interval of time (see Fig. 2), and (b) the fact that this decrease in Rn (0.06 μg . Ra equivalent from the 3rd to the 13th day) represents 70 per cent of the measured decrease in body burden within the same interval.¹² A similar relationship between exhaled Rn and excretion has been noted to follow injection of soluble Ra salts in dogs, and it is suspected to occur also in man following similar circumstances (9).

The elimination rate found by us after 100 days, however, is much greater than that found for the case of inhaled soluble salt (Fig. 10) and seems to be sustained at these levels by the mobilization of RaSO_4 from the lung. Indirect support for this hypothesis may be found in the following analysis: if λ is the fraction of lung burden mobilized per day, the actual amount made available daily to the body will be equal to $\lambda q_0 e^{-\lambda t}$, if q_0 is the total amount of Ra deposited initially in the lung. If this amount is assumed to behave thereafter as soluble Ra salt, then it will be excreted according to an expression of the type $\lambda q_0 e^{-\lambda t} \times A(T-t+1)^{-b}$, where $(T-t)$ is the time interval between pulmonary release and excretion, and A and b are the empirical constants found to describe correctly the elimination of soluble Ra salts in man. It follows, therefrom, that at any time, T , after inhalation the excretion rate dq/dt will be given by an integral of the type

$$\frac{dq}{dt} = \lambda q_0 A \int_{t=0}^{T-t} e^{-\lambda t} (T-t+1)^{-b} dt \quad (3)$$

We have evaluated this expression with $A = 0.5$, $b = 1.50$, $\lambda = 0.02$, and $q_0 = 0.248 \mu\text{g}$, the first two values in accordance with the data on man and the last two from

the lung activity of the particular individual in question (Fig. 7); the values expressed in per cent of the burden at 3 days are plotted in Figure 11 and are shown to be in reasonable agreement with the late phase of the experimental elimination curve.

It should be realized that this analysis cannot be expected to elucidate the actual mechanism involved in the transport of RaSO_4 from the lung. Thus, the exponential rate of disappearance, based on external activity of the lung, could represent either the rate of solubilization at the alveolar interface or rate of removal by macrophage transport. In the latter instance, the average life of the macrophage must be less than $1/\lambda \approx 34$ days in order to explain both the rate of disappearance from the lung and the availability of the Ra in soluble form. This statement applies only if Ra particles released by one macrophage are not phagocytized *de novo*. Lack of complete data on elimination in the Cincinnati cases precludes any statement as to the general success of the previous analysis. We may say only that the similarity in slopes in the retention curve (Fig. 3) of R. and K. to that of the case just described makes it plausible that the elimination curves of these persons might have resembled those shown in Figures 10 and 11. Unfortunately, the few data available, shown by the scattered points in Figure 10 at 1 day, 2 and 6 weeks,¹³ are at variance with this deduction and we are at loss to explain it.

We cannot refrain, however, from pointing out that if we assume that the skeletal Ra releases only radon, and this at the rate of 70 per cent of the Rn it produces, then it should be possible to calculate the bone deposition from the data of Table I. If this amount is subtracted from the body burden in each case, we obtain values which range from 1.6 to 3 times the total gamma-ray activity of the lung in cases R. and Ca., but more consistent with the

¹² On the assumption of a dry fecal sample of 25 gm., instead of 30, it would account for the total excretion observed for the same period.

¹³ We are indebted to Dr. D. S. Anthony for the values at 2 and 6 weeks.

lung activity of case G. The latter result merely confirms the assumptions made in the mathematical analysis, but the first two would indicate that a considerable fraction of the total burden is present neither in the skeleton nor in the lung, and is not being easily excreted. Possible sites are the macrophage population or the reticulo-endothelial system of the whole body. Alternative explanations for the data in question could be based also on a relatively low emanating power of radium sulfate in the skeleton and on gross error in the estimates of either total body or lung content.

SUMMARY

Six persons who suffered single accidental exposures to RaSO_4 dust were examined during the following year for exhalation of radon, and for gamma-ray activity from the thorax and from the body as a whole. Measurements of radium in the excreta of one individual have been obtained for about 250 days. Our observations reveal that the pattern of these measurements is radically at variance with observations made on human cases of chronic radium poisoning. In particular:

(a) The ratio of exhaled Rn to total Ra burden is distinctly lower, especially during the first six months.

(b) The gamma-ray scanning pattern easily discloses the sharp localization of the element in lung.

(c) During the first year, the gamma-ray activity from the thorax decreases with an average half-life of the order of 120 days.

(d) The elimination pattern found in a single individual is characterized by early elimination of Ra swallowed and a relatively high elimination at later times, presumably sustained by release of the salt from the lung.

We conclude, therefore, that estimates

of Ra body burden based solely either on radon or excretion measurements are likely to be seriously in error if applied to cases of recent exposure to insoluble dusts.

NOTE: The authors wish to express their indebtedness to Dr. A. M. Brues and Mr. J. E. Rose of this laboratory for continual help and encouragement during the course of these investigations.

P.O. Box 299
Lemont, Ill.

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(Para el sumario en español, véase la página siguiente.)

SUMARIO

El Transporte del Sulfato de Bario del Pulmón y su Eliminación del Cuerpo Humano a Continuación de Exposiciones Fortuitas Aisladas

A 6 personas que experimentaron exposiciones fortuitas aisladas a polvo de RaSO_4 se las examinó durante el año siguiente en busca de exhalación de radón y de actividad de rayos gamma procedente del tórax y del cuerpo en conjunto. Obtuvo mediciones de radio en los excrementos de un sujeto durante unos 250 días. Las observaciones revelan que el patrón de dichas mediciones discrepa radicalmente del de las observaciones ejecutadas en casos humanos de envenenamiento crónico por radio. En particular:

(a) La proporción de Rn exhalado a la carga total de Ra es netamente más baja, sobre todo durante los primeros seis meses.

(b) El patrón revelado por el escrutinio de los rayos gamma muestra fácilmente la

localización acentuada del elemento en los pulmones.

(c) Durante el primer año, la actividad de rayos gamma procedente del tórax disminuye con una semivida media del orden de 120 días.

(d) El patrón de eliminación observado en un solo sujeto se caracteriza por eliminación temprana del Ra ingerido y eliminación relativamente elevada en fechas subsiguientes, sostenida presuntamente por desprendimiento de la sal del pulmón.

Por lo tanto, dedúcese que los cálculos de la carga orgánica de Ra, basados exclusivamente en las mediciones ya del radón o de la excreción, son susceptibles de graves errores si se aplican a casos de exposición a polvos insolubles.

DISCUSSION

Eugene L. Saenger, M.D. (Cincinnati, Ohio): At the time of the exposure of the several individuals to radium as described in this excellent presentation, we were extremely fortunate in obtaining the services of the authors to carry out these precise and valuable determinations. This group at the Argonne National Laboratory has for some years pursued detailed studies on a large group of persons receiving large doses of soluble radium salts intravenously over long periods, and is thus especially qualified to explore this problem.

The study which is reported here is the first recorded description of acute exposure to a salt of radium as contrasted to chronic exposure, and the first description of the fate of insoluble particles of radium taken into the body as contrasted to the fate of soluble salts of radium given intravenously.

The 6 exposed individuals inhaled the radium in two accidents of similar nature. In each accident a 50-mg. sealed radium source with platinum walls was contained in a source housing. The source was raised from its lead shield to a platform by means of moderate air pressure from a hand pump. At the time of raising the radium in order to calibrate instruments, a fine white powder was seen escaping from the top of the housing.

The use of the scintillation counter for the de-

termination of retention of gamma-emitting isotopes was particularly helpful to us in separating the few contaminated individuals from a large group of suspects in a rapid and accurate manner. This method of measurement also demonstrated that only those individuals who actually saw the radium salt escape from the source housing suffered retention of radium. Many workers who were in areas of alpha activities of 2,000-3,500,000 d.p.m. for several days showed no evidence of radium retention after careful washing and complete clothing change. Considerable reassurance was obtained for those who had retention, since it could be rather accurately determined that the body burden was less than 1 μg . For reasons pointed out by the essayists, the method does not permit accurate localization of deposits within lung in so far as determining exactly what lobes are involved. The studies do suggest that RaSO_4 is either trapped in the pulmonary alveoli or passes through the gastroenteric tract without absorption.

There is one problem presented in this paper which is of considerable importance in our understanding of radium metabolism. This problem is the low level of radon found in the expired air as compared to the levels in those chronic cases in which solutions of radium salts were received intravenously. The radium sulfate which entered the lungs of these six individuals was pre-

pared as a coprecipitate with barium sulfate. O. Hahn¹ summarized in 1935 a series of experiments in which barium salts were precipitated from solutions using radium as a tracer. He showed that the radon was trapped in the crystal and that the smaller the crystal the greater was the emanation. When such a preparation was moist, the emanation increased from values of 0.3 per cent to several per cent. Also, when preparations of BaSO_4 which at 20°C . gave off 0.2 per cent of radon, were heated to 400°C . they gave off 0.8 per cent, and at 870° gave off 51 per cent of the radon. This effect following heating probably occurred as a result of the loosening of the crystal lattice of the coprecipitated BaSO_4 complex. These observations show that large amounts of radon are released from such particles only at very high temperature, and prove that the radium is retained as a solid particle rather than in solution. Therefore, the decrease in gamma emission from the thorax in these persons suggests actual removal of radium from the lung, and also from the body. Studies of particle size in the one accident were not successful, although such studies are extremely important in this general problem.

It is probable that there may be a greater tendency for the absorption into the blood stream and deposition in bone if radium chloride or radium bromide is the agent rather than the sulfate. No experimental evidence is yet available, to my knowledge, concerning the effects of ingestion or inhalation of particles of RaCl_2 or RaBr_2 .

We are certainly grateful to the authors for the very careful studies which they presented. Further valuable data can be obtained if similar future accidents are carefully studied in the manner described, especially in the first few days and

weeks. Only through such studies can an intelligent prognosis be given to exposed individuals. It is mandatory that we as physicians and physicists institute such studies as soon as similar accidents occur.

One might suppose that such accidents are rare. However, I should like to emphasize that in the last five years at least six known accidents involving the rupture of sealed sources have occurred. Each of these accidents has resulted in the expenditure of \$50,000 to \$100,000 for clean-up. It is, therefore, exceedingly important for all of us who use radium in any way to have a clear understanding of procedures to be instituted in case of rupture or spill.

Question: Where were the chronic cases obtained from?

Dr. Marinelli: Elgin State Hospital had a good group. Injections were given there about twenty years ago. We also had the splendid co-operation of practically every physician and hospital in Chicago. I may say that tracing patients is an art in itself.

Lauriston S. Taylor, Ph.D., Moderator: I would like to ask Dr. Marinelli a question. These accidents, of course, are never expected. If they were, they would not occur. I doubt that there are many places that are equipped as you are for carrying out studies of the sort which have been described. Should an accident occur, would it be possible to send the persons involved to you for initial observation and measurement?

Dr. Marinelli: We would be very interested to see them.

Question: Were any of the Cincinnati cases sent to Dr. Marinelli?

Dr. Saenger: Everyone who showed significant activity was studied by Dr. Marinelli.

¹ Hahn, O.: *Applied Radiochemistry*. Ithaca, N. Y., Cornell University Press, 1936. Chapters 9 and 11.



Detection of Intraocular Tumors with the Use of Radioactive Phosphorus¹

JACK S. KROHMER, M.A., CHARLES I. THOMAS, M.D., JOHN P. STORAASLI, M.D., and
HYMER L. FRIEDEL, M.D.

AT THE PRESENT time the most positive means of identifying malignant tissue is histologic examination. This is the method of choice and can be used in most situations. In the case of intraocular tumors, however, histologic confirmation is possible only after enucleation. It was therefore considered of great importance to utilize the selective localization of certain radioactive isotopes in tumors to aid in the diagnosis, *in vivo*, of such intraocular neoplasms.

It was known from earlier work (1-6) that various tagged materials are selectively taken up by rapidly proliferating tissue and that the increased radioactivity can be detected *in vivo* by specialized counting procedures. Application of this general method to the problem of identification of intraocular tumors was a logical extension. The problem was essentially one of differentiating between fluid detachment of the retina and detachments resulting from underlying malignant tumors. Although it is often possible to differentiate between these conditions by means of the usual diagnostic procedures (transillumination) and established criteria (presence of a retinal tear), many times such means are inadequate. It is in these cases that the present test has proved most valuable.

Since intraocular tumors are known to be adjacent to the outer surface of the eye, it is possible to use a beta emitter for their identification. The advantage in using beta rays is that the measurement obtained by counting directly over the suspected tumor is essentially unaffected

by the radioactive material in the surrounding normal tissue. Thus, the masking which might occur with a gamma emitter is avoided. P^{32} was chosen for the study because it had been shown by other investigators (1, 3, 6) to be taken up in tumor tissue in considerably higher concentrations than in normal tissue. It emits beta particles which have adequate penetration (8 mm. maximum in tissue)² and it has a half-life of sufficient length (14.3 days) to allow ease of handling and scheduling of patients.

METHOD

The method used at the present time is essentially the same as that reported by the authors in an earlier paper (7).

Counting Apparatus: Measurements over points anterior to the equator of the eye and points slightly posterior to the equator are made with a small end-window Geiger counter (Fig. 1).³ Preliminary work has been started on the development of a scintillation counter, which should allow counting directly over areas on the posterior half of the globe.

In Vivo Counting Procedure:

1. The patient is prepared by instillation of 1 per cent tetracaine hydrochloride or 4 per cent cocaine hydrochloride into the conjunctival sac.
2. A thorough ophthalmoscopic examination is carried out to determine the exact location and extent of the suspected tumor.
3. After a check has been made to determine that the counting apparatus is operating properly, 500 microcuries of

¹ From the Departments of Radiology and Surgery (Ophthalmology) of Western Reserve University, Cleveland, Ohio. Work performed under Contract No. W31-109-eng-78 between the United States Atomic Energy Commission and Western Reserve University.

Presented before the Thirty-eighth Annual Meeting of the Radiological Society of North America, Cincinnati, Ohio, Dec. 7-12, 1952.

² It should be remembered that the average range of the beta particle from P^{32} is only 2 mm.

³ Model 222, made by Anton Electronic Laboratory, Inc., 1226-1238 Flushing Ave., Brooklyn, N. Y.

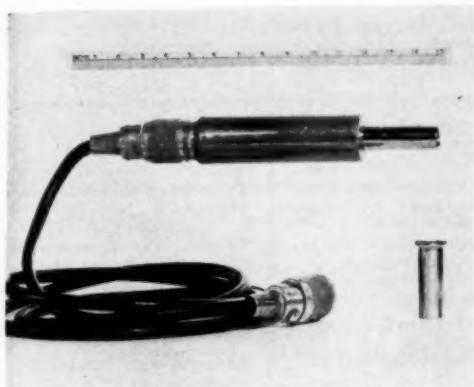


Fig. 1. Geiger counter used for *in vivo* P^{32} uptake measurements.



Fig. 2. Geiger counter shown in contact with eye during P^{32} uptake study.

P^{32} (in sterile isotonic saline) is injected intravenously.⁴

4. Immediately after injection, the counting procedure is started by placing the counting tube or crystal directly in contact with the eye, immediately adjacent to the suspected tumor (Fig. 2). Measurement is made for one-half to one minute in this location and the count is recorded. The counter is then moved to an unaffected portion of the eye (as far removed from the tumor site as is possible) and a similar count is taken. This procedure is continued by alternating the counting between the suspected tumor site and the normal tissue for approximately fifteen minutes. Additional counts are then made at one-half hour and one hour after injection.⁵

5. The variation in counts with time for the tumor and normal tissue are plotted on ordinary graph paper. The ratio of tumor to normal counts is determined for various times and is recorded.

⁴ 500 microcuries of P^{32} is far below the level of radioactivity which might produce manifest injurious effects. It is greater than the generally accepted "permissible dose." However, the exposure is less than that received during the course of most diagnostic x-ray procedures.

⁵ In most of the cases presented in this paper counts were made only at fifteen minutes, thirty minutes, and sixty minutes after injection. After experimental work on tumor uptake was carried out, it was observed that very early counting would be valuable.

In Vitro Counting Procedure:


















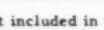

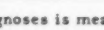

As soon as possible after enucleation, the eye is sectioned directly through the tumor. One half of the specimen is used for preparation of histologic sections and radioautographs. From the other half of the eye, samples of tumor, sclera, retina, and lens are obtained for assay of radioactivity.⁶ These aliquots are weighed wet and placed in porcelain counting dishes, dissolved in concentrated nitric acid and then dried, thus yielding thin, flat samples. After drying, the samples are counted under identical conditions, with a conventional laboratory Geiger counter apparatus. The results are recorded in corrected (for background radiation) counts per minute per gram of sample. The ratio of values for tumor to normal tissue is then determined, as shown in Table I.

RESULTS

A total of 32 cases, many with retinal separation and possible tumors, were studied. The results are shown in Table I, along with pathological and clinical findings for each case. The selective uptake has been recorded as the ratio of the count over the suspected site to that over a normal

⁶ It must be emphasized that counts should be made on fresh specimens. If these specimens are allowed to remain in a fixative for any length of time, there is a loss of activity from the sections by leaching.

TABLE I
TEST RESULTS FOR CASES WITH PROVEN* DIAGNOSES

Case No.	Date	Ratio of Tumor to Normal c/min		Disposition & Remarks	Pathological Findings (P) or Clinical Diagnosis (C)	
		In Vivo	In Vitro			
ANTERIOR TUMORS						
3	2-51		2.30	5.62	Enucleation for tumor	Melanoma of Choroid (P)
7	7-51		2.26	3.49	Enucleation for tumor	Melanoma of Choroid (P)
22	6-52		1.94	6.85	Enucleation for tumor	Melanosarcoma Choroid (P)
27	7-52		1.74	6.23	Enucleation for tumor	Melanoma of Choroid (P)
4	3-51		1.66	4.68	Enucleation for tumor	Melanosarcoma Choroid (P)
5	3-51		1.65	4.89	Enucleation for tumor	Melanosarcoma Choroid (P)
2	1-51		1.50	No Spec.	Enucleation for tumor	Melanoblastoma Choroid (P)
33	11-52		1.47	No procedure	No procedure	Metastatic Ca (Breast) (C)
9	9-51		1.42	No procedure	No procedure	Metastatic Ca (Breast) (C)
POSTERIOR TUMOR						
14	2-52		1.27	14.25	Enucleation for tumor	Melanoma of Choroid (P)
18	5-52		1.24	No Spec.	Enucleation for tumor	Spindle-cell Ca (P)
17	5-52		1.21	3.82	Enucleation for tumor	Melanosarcoma Choroid (P)
NON - TUMORS						
26	7-52		1.20	-	Operated for hemorrhage	Proven hemorrhage (P)
6	5-51		1.20	-	Reattached	Fluid detachment (C)
24	7-52		1.16	-	Enucleation for tumor	No tumor (P)
11	11-51		1.10	-	Reattached	Fluid detachment (C)
13	1-52		1.09	-	No procedure	Uveitis (C)
31	9-52		1.08	-	Reattached	Fluid detachment (C)
32	10-52		1.08	-	Reattached	Fluid detachment (C)
19	6-52		1.05	-	No procedure	Uveitis (C)
25	7-52		1.05	-	Reattached	Fluid detachment (C)
10	10-51		1.03	-	No procedure	Old healed inflam. les. (C)
8	9-51		1.02	-	Enucl. -sec. glaucoma	Uveitis (chronic) (P)
20	6-52		1.02	-	Reattached	Fluid detachment (C)
1	12-50		0.98	1.00	Enucleation for tumor	Fluid detachment (P)
30	9-52		0.95	-	Retina completely det.	Fluid detachment (C)
Measured, but not included in this table are: 2 probable anterior tumors refused enucleation, 4 possible posterior tumors not conclusive as yet.						
*By "proven" diagnoses is meant: 1. Definite pathological findings. 2. Successful reattachment. 3. Classical clinical findings.						

portion of the eye.⁷ The ratios for anterior segment tumors average 1.77. For anterior segment non-neoplastic lesions, the ratios average 1.07. For posterior neoplasms the average ratio is 1.24. In studying the figures, it would appear that a selective ratio of 1.4 or higher in the anterior segment is very suggestive of tumor, while a selective uptake ratio of less than 1.2 over the anterior segment strongly indicates a non-neoplastic process. As

⁷ The ratio used for the earlier studies is the average of the ratios at fifteen minutes, thirty minutes, and one hour. In the later studies the ratio used is the average ratio from the time of peak tumor reading to one hour. It should be noted that the ratio at one hour should not differ greatly from the ratio at fifteen minutes or at the tumor peak time if the results are to be considered indicative of tumor. Inflammatory lesions show very high ratios at early times, whereas at one hour the ratio in these cases has generally fallen to about 1.0. In cases where the ratio has decreased significantly by one hour, a three-day measurement should be carried out to assure valid results.

will be noted later, the uptake ratio for posterior tumors carries with it some uncertainty because of the difficulty in properly apposing the counter to the suspected site. In spite of this, the measurements for tumors in this region also appear significant.

Included in the series studied are 9 proved anterior tumors, 3 proved posterior tumors, and 14 non-neoplastic lesions. Six cases have not been tabulated, since it has not been possible to make a definite clinical or histologic diagnosis. In 2 of these 6 cases clinical changes and abnormal P³² uptake ratios (2.40 and 1.61) indicate probable tumors. The patients, however, have refused enucleation to date. The remaining 4 cases present posterior detachments for which preliminary measurements have been inconclusive.

In Cases 1 and 24, shown in Table I, clinical evidence pointed strongly to a neoplasm and thus, in spite of the fact that the P^{32} uptake fell within the non-tumor range, enucleation was performed. In both of these instances, histologic examination showed that no tumor existed. In Case 27 the clinical diagnosis appeared to be definitely that of a non-neoplastic fluid separation, and reattachment was attempted. After six weeks this proved to be unsuccessful and a P^{32} uptake study was done. The test showed an uptake ratio of 1.74. Because of the failure of the attempted reattachment and the increased P^{32} uptake over the suspected area, the eye was enucleated and a melanoma was found.

In the table, the lesions have been separated with reference to their position in the eye. This is necessary in order to examine critically the results which have been obtained.

In the case of an anterior segment process, the counter may be very closely apposed to the suspected area. In posterior sites, however, as noted previously, apposition is much more difficult and, in some cases, uncertain. In the evaluation of the results, therefore, it may be seen that anterior tumors gave clear evidence of a selective uptake whereas non-neoplastic lesions showed no essential elevation of the ratio of uptake. (It should be noted that all the non-neoplastic processes which were measured were in the anterior segment of the eye.) In the case of posterior tumors, the ratios are elevated, although only moderately. This may be due to the fact that satisfactory apposition to the tumor site was not possible. Therefore, an elevated ratio in suspected tumors in the posterior segment may be significant with our present method, but a low ratio, characteristic of non-tumors, may mean only unsatisfactory apposition and therefore unsatisfactory measurement.

An additional problem arises in the present method because of the relatively low levels of radioactivity which must be measured. With doses of 500 microcuries

of P^{32} , the measurements are generally in the vicinity of 300 to 500 counts per minute. Since the patients experience considerable discomfort with long measuring periods, the counting is best limited to approximately one minute or less. It is thus evident that the statistics of counting are relatively poor for a single measurement, and it is imperative that many measurements be made both over the tumor and over normal tissue to obtain valid results.

DISCUSSION

This study indicates that the measurement of P^{32} uptake in suspected intraocular tumors is of value in establishing the diagnosis. It is primarily effective in determining whether retinal separations are produced by neoplastic or non-neoplastic disease. There are many cases in which the appearance of a retinal lesion will permit satisfactory diagnosis by a trained ophthalmologist. There remain, however, numerous instances in which an elevation of the retina presents a difficult diagnostic problem. When the detachment is fluid in nature and a retinal tear can be identified, it may be considered strong clinical evidence that the lesion is due to a collection of subretinal fluid and is non-neoplastic in nature. In questionable cases, when a retinal tear is not found and when the appearance of the separation is not characteristic, the present test appears to be a very important aid in diagnosis. There is some question as to whether all patients presenting a retinal lesion should be examined by this method or whether a system of screening should be followed prior to study. All retinal lesions may be studied by this means, but there are many conditions which may be clearly identified without its aid as non-neoplastic in nature, e.g., choroiditis.

The success of the test is largely dependent upon determination of the exact location of the separation and the site of the suspected tumor. Ophthalmoscopic examination must be carried out under the effect of a mydriatic in order to permit the most careful localization. Since the

maximum range of the P^{32} beta particles is about 8 mm. in tissue, it is necessary to be certain that the counter is in as close proximity to the tumor as possible. For practical purposes, 5 mm. or more between the tumor and counter is very unsatisfactory. Therefore, when difficulty in

over the tumor and over normal tissue were made. These measurements were continued for a period of one or two hours. Additional counts were taken the following day and at subsequent times up to three or four days. A graph showing the composite variation of counts with time

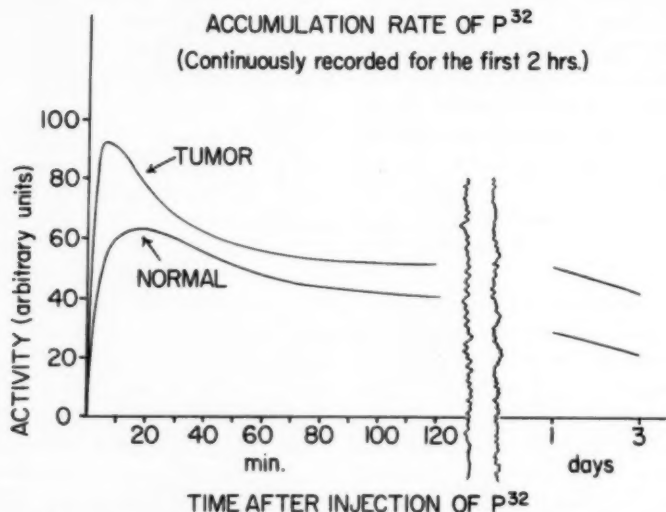


Fig. 3. Accumulation rate of P^{32} . Curves show uptake of P^{32} in tumor and in normal tissue as a function of time after injection. Curves are composite of two cases: skin metastases from a carcinoma of the breast and of the stomach, respectively.

properly placing the counter in close apposition to the tumor is experienced, the significance of the result, particularly if it be a negative one, is doubtful. It thus becomes very difficult to study tumors situated in the posterior quadrants, since the Geiger probe described above is applied with considerable uncertainty in that portion of the globe.

The present test differs from previous tumor studies with P^{32} in that measurements are made within a very short period of time following injection rather than after two to four days. Preliminary studies were made of the early accumulation rate of P^{32} in neoplastic and normal tissue. A number of patients with superficial malignant tumors were studied, using the following procedure. Immediately after the injection of a 500-microcurie tracer dose of P^{32} , continuous recordings of counts

was prepared from these data and is reproduced here as Figure 3. Examination of this curve shows that at a very early time (less than fifteen minutes for the patients studied) the ratio of tumor counts to normal counts reaches a maximum, and that this ratio decreases for one or two hours following injection. After this decrease, a subsequent increase in ratio becomes evident and continues over the periods studied, probably reaching a maximum in four or five days. The cause for increased activity in the tumor tissue at an early stage is uncertain⁸ and is now under further investigation.

⁸ It may be due to one or all of the following: (1) increased vascularity of the tumor; (2) more rapid transport of the inorganic phosphorus across the vascular membrane into extracellular space; (3) more rapid transport of the P^{32} across cellular membrane into intracellular space; (4) more rapid incorporation of P^{32} into nuclear and other cellular constituents.

Although we have examined 32 cases, the results must still be used with considerable caution. It is certainly not intended to propose that the selective uptake of P^{32} in tumors be utilized as a substitute for a thorough and careful clinical examination of a patient with a suspected intraocular tumor. However, from the data which we have obtained, it does appear to be a valuable adjunct. The work is to be continued with special emphasis on the development of a counter which will permit satisfactory measurements over the posterior segments of the globe. Complete understanding of the usefulness of the test must await much more extensive application.

SUMMARY

Thirty-two cases of various intraocular lesions have been studied. Measurement of the differential uptake of P^{32} in tumors appears to afford a clear separation of neoplastic from non-neoplastic disease. This is most effective in the anterior segment.

To establish the diagnosis in neoplasms located in the posterior portion of the globe, a counter which will permit closer apposition to the tumor will be necessary.

The results of the P^{32} uptake studies

must be considered as an adjunct to careful clinical evaluation of suspected eye tumors rather than a conclusive diagnostic test.

2549 Edgehill Road
Cleveland 6, Ohio.

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(For Discussion of this paper, see page 938.)

SUMARIO

Descubrimiento de Tumores Intraoculares con el Uso de Fósforo Radioactivo

El método descrito permite diferenciar las neoplasias de otras lesiones intraoculares. Después de la inyección intravenosa de 500 microcuries de P^{32} (en solución isotónica estéril), se hacen mediciones con un contador Geiger, puesto directamente en contacto con el ojo y adyacente al tumor sospechoso. Luego se hacen mediciones sobre una zona indemne del ojo y se determina la proporción que existe entre la medición sobre el tumor y la obtenida sobre la porción normal del ojo.

Para los tumores del segmento anterior del ojo, se observó que la proporción promediaba 1.77 y para las lesiones no neo-

plásicas, 1.07. Para las neoplasias del segmento posterior, la proporción es de 1.24. Esta proporción más baja, se considera debida a la dificultad experimentada para colocar el contador en aposición exacta en las lesiones del segmento posterior. En los tumores de esta zona, aunque un coeficiente elevado puede revestir importancia, un coeficiente bajo resulta, por consiguiente, poco terminante.

El resultado de los estudios de absorción de P^{32} debe considerarse como un auxiliar de la cuidadosa justipreciación clínica de los tumores oculares sospechosos más bien que como prueba terminante de diagnóstico.

Intracavitary Use of Colloidal Radioactive Gold¹

GOULD A. ANDREWS, M.D., SAMUEL W. ROOT, M.D., RALPH M. KNISELEY, M.D., and
HERBERT D. KERMAN, M.D.

AMONG THE radioisotopes which have therapeutic value is radioactive gold, Au¹⁹⁸. It has a half-life of 2.8 days and decays with both beta and gamma emissions. One peculiar advantage of this element is that it can be prepared as a colloid which is chemically stable and rela-

of the present discussion. This use for the isotope was first suggested by J. Muller (4), of Switzerland.

During the last two years our group at the Oak Ridge Institute has been carrying on a program of experimental treatment with radioactive colloidal gold. The pres-

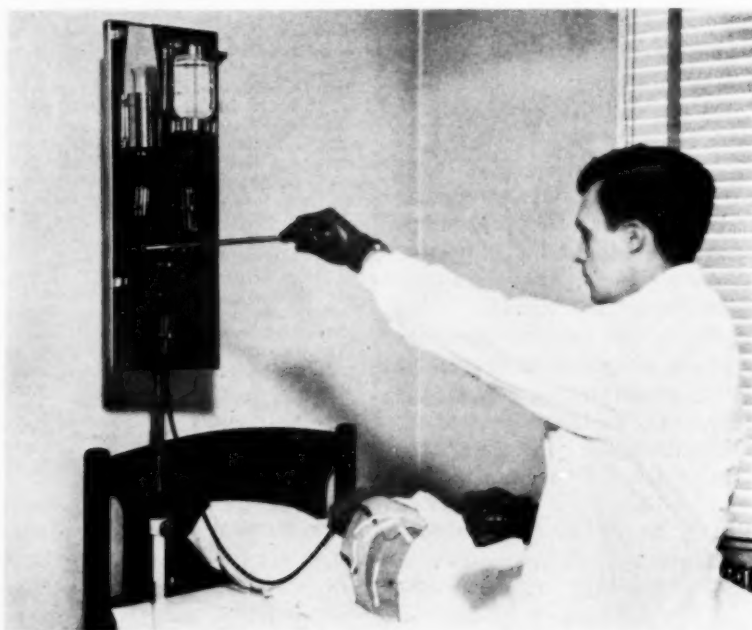


Fig. 1. Photograph taken during the intrapleural administration of radioactive colloidal gold. Personnel radiation hazard is minimized by the use of a simple gravity infusion device. Clamps controlling rate of flow, dilution, and rinsing with saline are adjusted by means of a special long-handled wrench.

tively inert biologically. Dr. Paul Hahn, of Meharry Medical College, has introduced the use of this isotope for direct injection of tumors and intravenous administration (1, 2, 3). Its value as a means of irradiating body cavities for the control of fluid accumulation is the subject

ent discussion is based largely upon material which has already appeared in other publications (5-8). We have injected the isotope into pleural and peritoneal spaces of patients with effusions caused by neoplasms and have attempted to study its fate, distribution, and effects.

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Some of the patients treated have been relatively unsuitable, having advanced disease with such complications as mediastinal compression and impending intestinal obstruction. In some of these more unfavorable cases, the need to collect information, as well as the rather distant

those used for giving intravenous fluids. Physiological saline, 200 to 400 ml., is used for rinsing. The operator receives radiation doses far below tolerance. The method of administration is illustrated in Figure 1.

During the first few hours after the gold

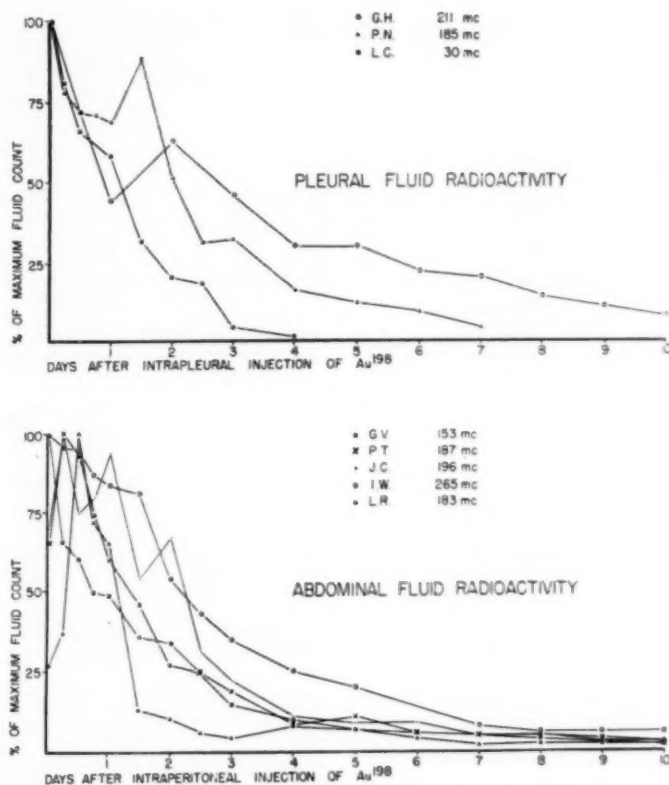


Chart I. The radioactivity of the fluid of cavities after treatment with radioactive colloidal gold. There is a pronounced early fall in concentration of the isotope, probably due chiefly to adsorption on serous surfaces. All values are corrected for radioactive decay. Reprinted, by permission, from *Cancer*, March 1953.

hope of improvement for the patient, was a reason for giving the treatment.

In administering the isotope, we have usually aspirated a considerable portion of the fluid, inserted a polyethylene tube through the needle used for aspiration, removed the needle, and then allowed the radioactive colloidal gold to flow through the tube into the cavity. This procedure requires a simple infusion device similar to

has been given, the patient is asked to move about frequently to aid free mixing in the cavity. There is a tendency for the gold in the pleural cavity to settle in the costophrenic angles and for that in the peritoneal space to concentrate in the pelvic region. It is important, therefore, for the patient to be in a head-down position at least part of the time immediately after administration.

The optimal dosage of gold has yet to be determined. We have employed various amounts, including some that were probably larger than necessary. Most of the patients treated recently have been given 150 mc. for ascites and 75 mc. for pleural effusion. In a few cases we have repeated

cult to find near the treated cavities, and lymph nodes replaced by neoplasm have shown very little radioactivity.

Small but measurable amounts of radioactivity are found in the blood soon after the gold is injected. In some patients the blood level reaches a maximum on about

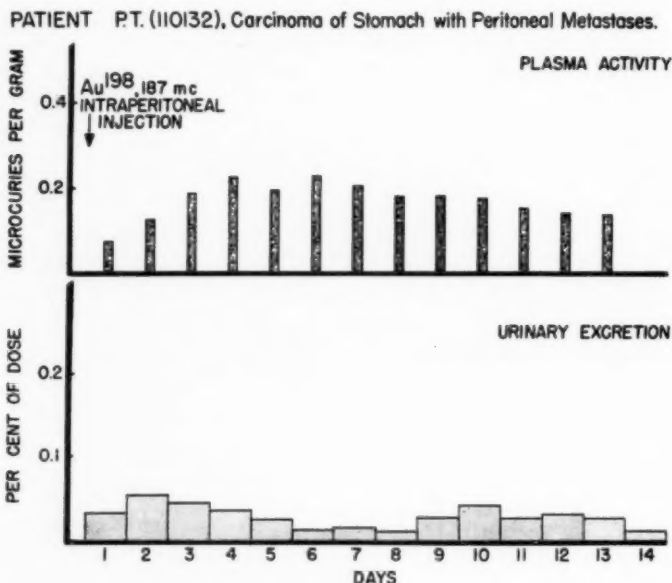


Chart II. Graph indicating blood and urine levels of radioactivity in a typical patient after a single intraperitoneal injection of colloidal radioactive gold.

the treatment of the same cavity several weeks after the initial dose. When more than one cavity is to be treated in the same patient, the injections are given separately, with intervals of a few weeks, and individual doses are sometimes reduced so that the total will not be excessive.

After the gold is injected, its concentration in the fluid of the cavity decreases rapidly during the first three or four days, as shown in Chart I. Most of this early decrease appears to be due to simple adsorption of the colloid on the serous surfaces of the cavity. Aggregates of gold are found in large phagocytic cells in the fluid, on the serous surfaces, and beneath the surfaces. Our studies on lymphatic distribution have not been very satisfactory. Normal nodes have been diffi-

cult to find near the treated cavities, and lymph nodes replaced by neoplasm have shown very little radioactivity. Small but measurable amounts of radioactivity are found in the blood soon after the gold is injected. In some patients the blood level reaches a maximum on about the third day and then remains almost stationary for several days. In other patients the blood level continues to rise gradually for ten days or so. The amount of the isotope in the blood stream at any one time is always less than 1 per cent of the dose given, but the blood may transport considerably more than this from the cavity. Urinary excretion is very slight. Much less than 1 per cent of the total dose can be recovered from the urine. After the first two or three days the amount in the urine parallels the blood level, but initially the urinary excretion is somewhat higher in relation to the blood. This may reflect the presence of a very minute amount of ionized gold in the blood. Chart II illustrates levels of radioactivity in the blood and urine of one patient.

Autopsy studies of liver, spleen, and bone marrow after intracavitary administration of colloidal gold indicate that a variable amount reaches these organs, and that the total may be as much as 15 per cent of the initial dose. Perfusion studies by Little (9) have shown that in



Fig. 2. Autoradiogram made from a slice of liver obtained at autopsy six days after 10 mc. of colloidal radioactive gold were given intraperitoneally. There is an uneven deposition of the isotope on the surface. Within the organ there is more uniform distribution, presumably resulting from the blood-borne fraction of the radiogold deposited in reticulo-endothelial cells. The large pale area in the upper part of the specimen is at the site of a metastasis.

the dog about 90 per cent of the gold in the blood is removed with the first passage through the liver. The transportation of a fraction of the isotope from the cavity to these organs occurs gradually, and is not complete until several half-lives have passed. Figure 2 shows peritoneal sur-



Fig. 3. Autoradiogram of a slice of spleen obtained at autopsy sixteen days after 78.4 mc. of radioactive colloidal gold were injected intrapleurally. There is a diffuse deposition of the blood-borne colloid, with additional punctate areas of darkening which may indicate aggregation into larger particles.

face adsorption and parenchymal distribution in the liver, and Figure 3 shows the distribution in the spleen after intrapleural injection. The concentrations of radioactivity in the bone marrow are usually much lower than those in the liver and spleen but, because of the radiosensitivity of the marrow, this appears to be the most important site of possible radiation damage.

Hematologic effects are quite definite but have never been severe enough to be alarming. A few patients have an initial leukocytosis, which may be a response to local inflammation around the cavity.

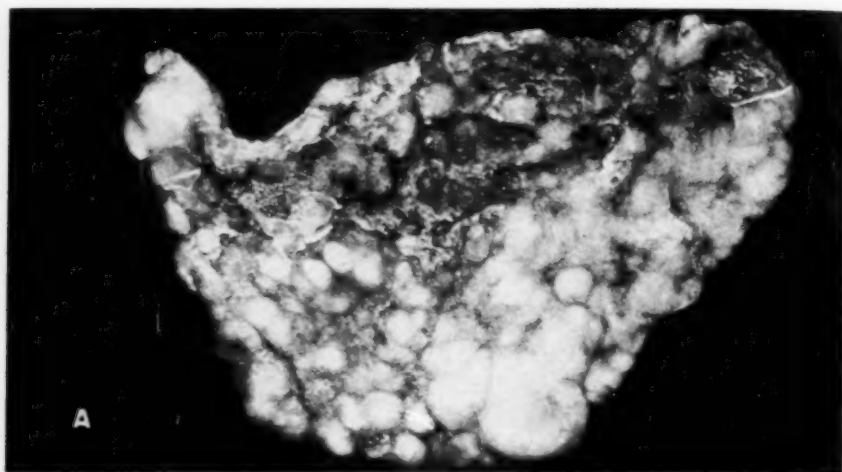


Fig. 4A. Photograph of area of peritoneum from a patient with widespread carcinomatosis.

In all patients given moderate or large doses, there is a series of gradual changes in the blood and marrow of the type seen in total-body irradiation, with subsequent recovery. When the number of lymphocytes in the blood is not already greatly diminished because of reaction to the neoplasm, a prompt lymphopenic response to the isotope treatment develops. In some of our patients given rather large doses, the total leukocyte count was temporarily depressed to the neighborhood of 2,000 per cubic millimeter. These effects upon hematopoiesis may be due to the radiation from the small amount of the isotope which is absorbed and deposited in the marrow. Another important factor may be the gamma radiation which reaches the marrow from the large proportion of the isotope which remains localized in the region of the cavity of injection. The relative importance of the radiation from these two sources is not known.

After the administration of the gold, there is frequently a mild clinical reaction to the treatment. Some patients have nausea and vomiting from about the second to the fourth or fifth day after treatment, and diarrhea occurs in a few individuals. These effects are more likely to be associated with larger doses and are more frequent following intraperitoneal than fol-

lowing intrapleural administration. We believe that these symptoms represent true radiation sickness.

The effect of treatment on fluid accumulation is gradual. A few weeks often pass before a decrease in the rate of accumulation is observed, and even the patients who ultimately have good results usually require one or two paracenteses after the isotope is given.

It has been believed that the therapeutic effect results chiefly from the beta radiation of the gold. There is as yet no evidence of selective placement on neoplastic surfaces, and the deposition of the gold is generally quite uneven, as shown in Figure 4. The beta radiation from the gold which remains suspended in the fluid is essentially shielded out, and therefore ineffectual, except for that very close to the interface of the fluid and serous surface. Chamberlain (10) has calculated that with 100 mc. deposited on 30,000 sq. cm. of serous surface (as might occur after an intraperitoneal dose of the magnitude used in the present study) there would be an effective beta radiation immediately beneath the surface of 3,000 equivalent roentgens. Because of the lack of penetrating power of this beta particle, its dosage more than 3 mm. below the surface is negligible.

Relatively little has been said about

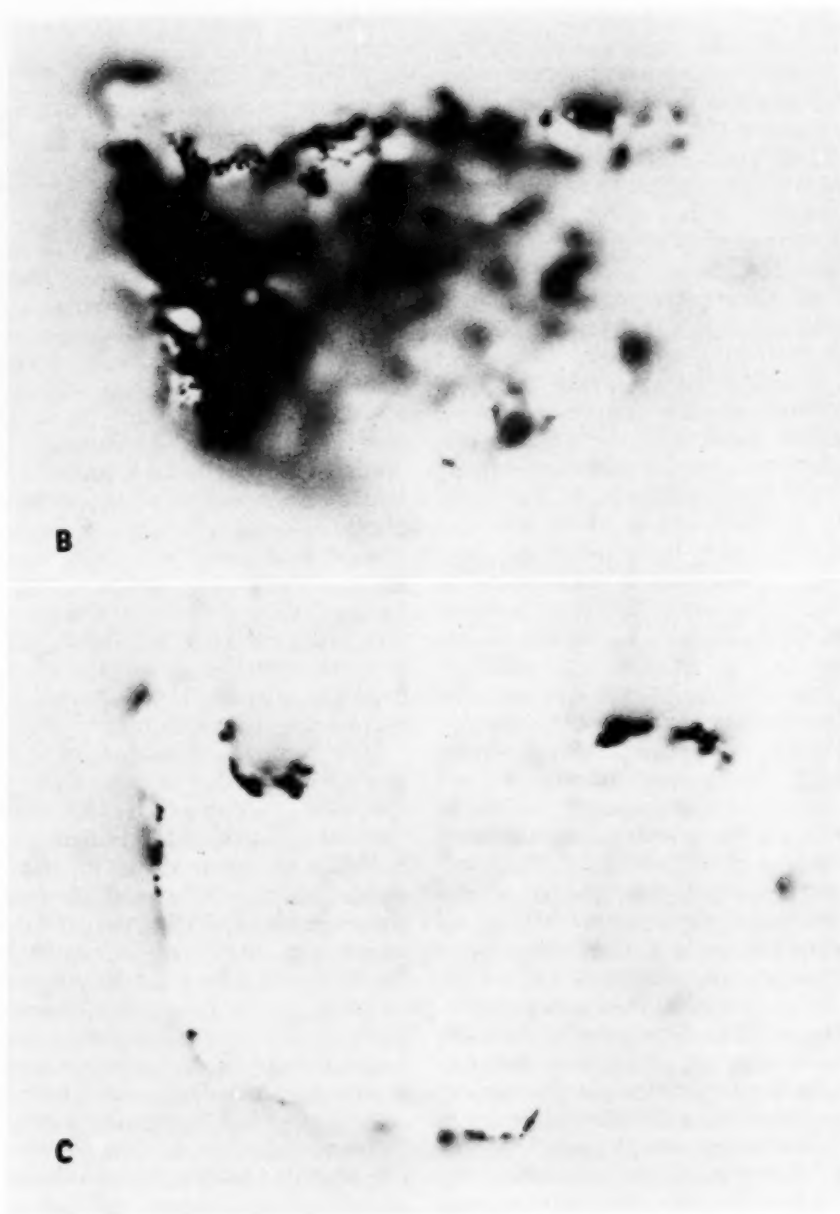


Fig. 4B and C. B. Autoradiogram prepared from surface of the specimen shown in Fig. 4A. Because of the uneven thickness of the tissue, contact with the film was not uniformly good, and this is the reason for the indistinct image. An uneven distribution of the gold is indicated, and there is some suggestion that the neoplastic surfaces hold less of the isotope than the normal. C. Autoradiogram made from the under surface of the same specimen. The tissue shields the film from the superficially placed radiogold, and the chief darkening is at the edges, where some folding allows contact of the peritoneal surface with the film.

the importance of the gamma emission from the gold. At the serous surface it is insignificant compared with the beta radiation, but at areas more than a few millimeters beneath the surface it is the chief source of radiation. We do not yet know how much it contributes to irradiation of lymph nodes, liver, spleen, and bone marrow as compared with the beta radiation from the small amount of isotope carried to these sites. Because of the increasing use of this isotope and because of some prevalent misconceptions about the resulting tissue dosage, there is a need for experimental data on this problem. Calculations based upon the radiation distribution after direct injection of tumors are not directly applicable to the intracavitary problem. It is likely that the gamma emission is more important than has been realized, and if the therapeutic effect is chiefly that of the beta emission, then the gamma may be distinctly undesirable because of the total-body irradiation produced.

The mechanism of action of this therapy is not known. Cytologic studies of pleural and ascitic fluids after treatment have shown apparent disappearance of malignant cells in a few cases but, because of the uncertainty of finding such cells, the significance of this is questionable. In several cases malignant cells persisted in the fluid after treatment, and some of these patients had a good result in terms of a great decrease in the amount of fluid accumulation. Autopsy studies have shown variable degrees of fibrosis of serous surfaces. This fibrosis was usually not pronounced and did not appear to contribute to intestinal obstruction except possibly in one patient who was given unusually large doses. In several patients areas of actively growing neoplasm were present on and near the serous surfaces, and any inhibition of tumor growth by the isotope was questionable and limited to a most superficial position.

In selecting patients for intracavitary gold treatment, the physician should keep in mind that at present the only demon-

TABLE I: SHORT-TERM RESULTS OF TREATMENT IN 39 CASES

Cessation of, or distinct decrease in, fluid accumulation.....	16
Some decrease in fluid.....	7
No effect on fluid.....	2
Unsuitable for evaluation because of early death from neoplasm.....	10
Unsuitable for evaluation because of combined therapy.....	4

strated value of the therapy is in the control of fluid. If effusion is only incidental, and not a chief cause of symptoms, benefit should not be expected. In our experience, ascites alone is not a cause of intestinal obstruction, and in patients showing symptoms of obstruction due to metastatic neoplasm this form of treatment does no good. The most suitable patients for this therapy are those who have no large neoplastic masses, who are maintaining fair general health, and whose only symptoms are those related to the presence of fluid accumulations. We have also felt that it may be worth while to evaluate the effect of treatment of patients with fine miliary neoplastic seeding of the serous surfaces, even in the absence of fluid.

It is our opinion that x-ray therapy is less effective than intracavitary gold in controlling effusions due to metastatic carcinoma, and that the isotope treatment is preferable when control of fluid is the only objective. When x-ray therapy offers some chance of slowing the growth of the tumor and, therefore, prolonging the patient's life, it should not be supplanted by colloidal gold. In suitable cases, intracavitary gold treatment can be combined successfully with deep x-ray therapy of a local area of neoplasm, and it may be possible to give full therapeutic doses of both forms of radiation. Patients with pleural effusions due to lymphoma sometimes respond to intrapleural gold, but x-ray therapy of the mediastinal lymph node areas is believed to be preferable as an initial treatment.

Some consideration has been given to prophylactic use of this treatment in patients found to have apparently resectable tumors of a type frequently associated with later peritoneal or pleural

involvement. In such cases, the possible benefit in increased survival rates must be weighed against undesirable late radiation sequelae (such as an increased incidence of leukemia), which might occur in patients cured of their original neoplasm by surgery.

The results of our clinical experience in 39 cases, up to the present, are summarized in Table I. The condition of the patient after treatment depended on the extent and course of the neoplastic disease, which was apparently not modified by the treatment, except for the effect upon effusions.

P.O. Box 117
Oak Ridge, Tenn.

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(For Discussion of this paper, see page 938.)

SUMARIO

Uso Intracavitario del Oro Radioactivo Coloidal

Después de inyectar oro radioactivo (Au¹⁹⁸) en los espacios pleurales y peritoneales de enfermos que tenían derrames debidos a neoplasias, estudiáronse el destino, distribución y efectos del mismo. No se ha determinado todavía la dosis óptima. En la mayor parte de los enfermos tratados recientemente, se administraron 150 mc. para ascitis y 75 mc. para derrames pleurales.

Poco después de la inyección, descubriéronse en la sangre cantidades pequeñas del isótopo. La excreción urinaria es escasa. Al hígado, bazo y médula ósea llega una cantidad variable.

Los efectos hematológicos son bastante bien definidos, pero jamás de tal intensidad

que sean alarmantes. Obsérvase frecuentemente una leve reacción clínica al tratamiento, que se considera que representa verdadera enfermedad por irradiación.

El único valor demostrado de esta terapéutica radica en el dominio del derrame, para lo cual creen los AA. que la inyección de oro radioactivo es superior a la roentgenoterapia. El proceso neoplásico no se modifica aparentemente. Si el derrame es puramente incidental y no ocasiona síntomas, no cabe esperar beneficio.

Entre 39 casos, logróse cese o disminución precisa del líquido en 16 y alguna reducción en 7. No se observó efecto alguno en 2 casos y los demás no se prestaban para justipreciación.

The Hepatic Radioactivity Survey¹

LLOYD A. STIRRETT, M.D., ERIC T. YUHL, M.D.², and RAYMOND L. LIBBY, Ph.D.

IT IS THE purpose of this communication to report our experiences with the hepatic radioactivity survey for the diagnosis of cancer of the liver. The technique of the procedure and the results in a preliminary series of 65 patients have been described in a previous publication (2).

The radioactivity survey has been performed on a total of 210 patients to date and has proved to be more accurate and reliable for the diagnosis of hepatic metastases than either liver-function test or needle biopsy of the liver. Iodinated human serum albumin (I^{131} HSA) has been employed as the tracer agent, and the scintillation counter as the detector of the gamma quanta emanating from the I^{131} .

METHOD

The I^{131} HSA used in this study was obtained from Abbott Laboratories. I^{131} has a half-life of eight days and emits a gamma ray sufficiently intense to be recorded externally by the scintillation counter. Radioactive human serum albumin has been used extensively in other investigations (5), and no toxic effects have been encountered from its use in the doses required for radioactivity tracer surveys. I^{131} HSA is a homologous serum protein and contains 5 mg. of human serum albumin per millicurie of solution (3).

The wide-angle scintillation counter (1) has been modified for this application by adding 2.5 cm. of lead around the sides of the tube and 3 cm. of lead around the bottom of the tube, leaving a 3/4-inch aperture. This additional shielding minimizes background gamma radiation from parts of the body other than that under survey and is essential for the success of the



Fig. 1. The scintillation counter is shown mounted on the portable x-ray unit. Note the perforated guide on the patient's abdomen.

procedure. It also provides collimation so that the incident angle of radiation is limited to approximately 30 degrees. The counter is mounted on a portable x-ray unit with a special adapter in order to facilitate positioning of the tube during the survey (Fig. 1).

The patient is given a single sterile intravenous dose of 300 microcuries of I^{131} HSA, in an average volume of 2 c.c. Twenty-four hours after the injection the patient is placed upon an ordinary examining table and a careful abdominal examination is done to determine the

¹ From the Surgical Service and Radioisotope Unit, Wadsworth Hospital, Veterans Administration Center, Los Angeles, and the Departments of Surgery and Radiology, School of Medicine, University of California at Los Angeles. Presented at the Thirty-eighth Annual Meeting of the Radiological Society of North America, Cincinnati, Ohio, Dec. 7-12, 1952.

² Research Fellow, U. S. Public Health Service, National Institute of Neurological Diseases and Blindness.

anatomic location of the costal margins, the xiphoid process, the liver edge, and any palpable masses or organs. With the aid of a perforated guide centered over the xiphoid process, co-ordinate rectilinear points are marked on the patient's skin at intervals of 5 cm., extending from the nipple line to below the umbilicus and from flank to flank. A total of 42 points are thus marked and the guide is removed.

The aperture of the tube is placed flush with the patient's skin and successive counts are obtained at each point. Care is taken to maintain the counter perpendicular to the long axis of the body at all times. A sufficient number of counts are observed at each point to insure a counting error of less than 3 per cent.

Approximately 5 per cent of the radioactive iodine contained in the I*HSA is present as free iodide and may be absorbed by the thyroid gland. In order to preclude an untoward effect upon thyroid function by absorption of this free iodide, 0.5 c.c. of potassium iodide as Lugol's solution is administered to the patient three times a day for four days, beginning twenty-four hours prior to the survey. In those cases where oral administration is not feasible, sodium iodide may be injected intravenously in place of the Lugol's solution.

The maximum concentration of the I*HSA in the blood stream is observed immediately after injection, and in twenty-four hours after the injection a stable level of activity is present. Accordingly, the survey is routinely performed at the twenty-four-hour interval in order to avoid errors which might arise because of changes occurring during the test period. Repeated surveys may be carried out at intervals of forty-eight and seventy-two hours after injection in order to confirm the presence of an area of abnormal radioactivity. At the ninety-six-hour interval, insufficient activity is present for a survey.

RESULTS

The normal range of radioactivity was first determined in a series of 20 carefully

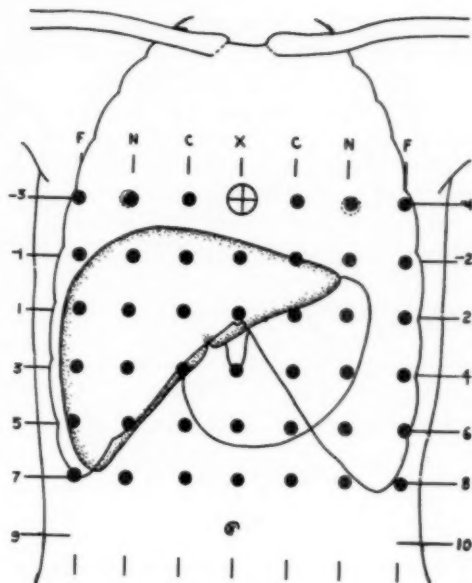


Fig. 2. Sketch of the 42 coordinate points in relation to the anatomic landmarks. Note the X position on the -3, -4 line, which is used as the point of reference.

selected control patients. Liver diseases and complicating systemic diseases were excluded in these patients by full history, physical examination, and laboratory studies, including tests of liver function. Abdominal radioactive surveys were then carried out in accordance with the technic described.

The radioactivity observed at the X position on the -3, -4 line was arbitrarily chosen to represent 100 (Fig. 2). The radioactivity values in terms of counts per second at each of the remaining points were then expressed as a percentage of the count observed at the X -3, -4 position. The standard deviation of these values was determined for each of the co-ordinate points and was multiplied by a factor of 1.5.

The values thus obtained (1.5 standard deviations on each side of the mean) represent the range within which approximately 90 per cent of the observations on normal patients will be expected to fall. Therefore, in the subsequent surveys on patients suspected of having liver metastases, any

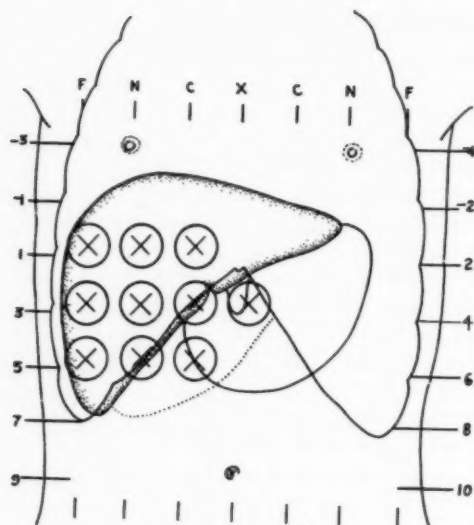


Fig. 3. Anatomic sketch showing foci of abnormal radioactivity observed over the region of the liver in a patient with verified hepatic metastases.

value beyond this range was considered abnormal. The type of data obtained in this study does not warrant a more precise statistical treatment, and it is found that this approximate method of analysis is adequate for selecting abnormal values.

In the preliminary series (2), the xiphoid position (X, 1, 2) was used as the point of reference to express the amounts of radioactivity at the remaining positions. It was observed, however, that in 3 patients with proved metastases in the region of the xiphoid process, false negative results were obtained. In order to avoid errors arising as a result of increased radioactivity at the point of reference, the X -3, -4 position was substituted for the X 1, 2 position as the point of reference in all of the subsequent surveys.

Abdominal radioactivity surveys were performed on a total of 151 patients who had proved primary neoplasms.

Group A: In 119 of the 151 patients with proved neoplasms, the liver appeared to be grossly normal at the time of laparotomy and there was no visible or palpable evidence of hepatic metastases. The radioactivity surveys were within the

control ranges in 114, or 96 per cent, of this group. Twenty-two of these patients have died, and careful serial sections of the liver revealed no evidence of metastases.

Group B: In 32 patients, hepatic lesions were found at operation. Biopsy of the liver and microscopic examination confirmed the presence of metastases. The abdominal radioactivity surveys performed before operation revealed foci of abnormal radioactivity in 30 (94 per cent) of the patients.

For purposes of anatomically orienting the location of the abnormal foci of radioactivity, the points at which they occurred were recorded on a simple anatomic sketch representing the location of the co-ordinate points in relation to the underlying viscera (Fig. 3).

DISCUSSION

Liver-function tests and needle biopsy of the liver are the procedures currently used to detect hepatic metastases. These procedures are often unreliable and the findings inconsistent (4). In our series, the liver-function tests were abnormal in less than 40 per cent of the 32 patients who had verified hepatic metastases. The variations observed in the liver-function tests were non-specific, and in many instances of advanced metastatic neoplasms, only a single test in the liver panel was abnormal.

False negative results are frequently obtained by liver biopsy. In addition, this procedure is hazardous, since it may cause intraperitoneal hemorrhage or biliary peritonitis.

The presence of icterus is felt by many clinicians to contraindicate liver biopsy since biliary peritonitis is more frequent under such circumstances. Jaundice also interferes with the interpretation and reliability of many of the liver-function tests. The hepatic radioactivity survey, however, is neither contraindicated nor unreliable in the presence of icterus.

Twenty-eight patients with various benign liver diseases were surveyed in order to determine the influence of such condi-

tions upon the radioactivity test. Fourteen of the 28 patients had cirrhosis with various degrees of jaundice but no ascites. Values within the normal range were observed in each case. Eight of the 28 patients had advanced cirrhosis with ascites. Abnormal radioactivity surveys were obtained in 6 (75 per cent) of the 8 patients. The remaining 5 patients had acute hepatitis and an abnormal survey was obtained in only 1 instance. These observations indicate that cirrhosis with or without jaundice does not influence the test but that the presence of ascites interferes with the interpretation of the survey. In patients with acute hepatitis, abnormal surveys may occasionally be obtained.

The radioactivity survey has been performed on 151 patients with primary carcinoma. Thirty-two of these patients had metastatic hepatic carcinoma proved by liver biopsy at the time of operation. Radioactivity surveys on these 32 patients before operation revealed foci of abnormal radioactivity in the region of the liver in 30 (94 per cent). Two false negative results were obtained in this group. In the remaining 119 patients no evidence of hepatic metastases was found at operation. Surveys were normal in 114 (96 per cent) of this group. There were 5 false positive results. Thus, an overall diagnostic accuracy of 95 per cent was attained in 151 patients with proved carcinoma.

The hepatic radioactivity survey offers a reliable means of detecting liver metastases in the many instances where the peritoneal cavity is not entered and the liver is not accessible for evaluation. It also alerts the surgeon to the presence of hepatic metastases in the instances where radical extirpation of a neoplasm is contemplated.

(For Discussion of this paper, see page 938.)

SUMARIO

Exploración Radioactiva del Hígado

Descríbese una técnica para el reconocimiento del hígado en cuanto a radioactividad, por medio de un cuentachispas mo-

The radioactivity survey has proved to be far more reliable for these purposes than the tests heretofore available. Surveys are also of use in the evaluation of the post-operative course of the cancer patient, since they often warn the clinician of the recurrence of neoplastic disease before such recurrence may be otherwise detected.

The abdominal radioactivity survey is now used routinely on the surgical service of the Wadsworth Hospital (Los Angeles) both in the preoperative evaluation of all patients with suspected carcinoma and the follow-up examinations of these patients after operation.

SUMMARY

The technic of hepatic radioactivity survey for the diagnosis of metastatic cancer of the liver has been described.

A series of 210 patients have been studied and an overall diagnostic accuracy of 95 per cent has been obtained.

ACKNOWLEDGMENT: The authors wish to express their gratitude to Miss Doris Donohue of the Surgical Research Laboratory for her co-operation and assistance in this study.

11333 Kiel St.
Los Angeles 49, Calif.

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dificado de ángulo ancho, después de la inyección intravenosa de seroalbúmina humana yodada.

Con la ayuda de una rejilla perforada, centrada sobre el cartílago xifoides, se marcan en la piel del enfermo cuarenta y dos puntos rectilíneos coordinados a distancias de 5 cm., haciéndose mediciones en cada punto. Se determinó la escala normal de radioactividad, para una serie de 20 personas normales, considerándose como anormal todo valor que se separa de dicha escala.

Ejecutáronse reconocimientos en 151 enfermos que tenían carcinoma primario, en 32 de los cuales había metástasis hepáti-

cas, según se comprobó con la biopsia al operar. En todos los de este último grupo, menos 2, la exploración con la técnica aquí descrita, reveló, antes de la operación, focos de radioactividad anormal en la región hepática. En 119 no se descubrieron signos de metástasis hepática al operar, y en este grupo sólo hubo 5 resultados seudopositivos con la técnica en cuestión, lo cual representa una exactitud diagnóstica global de 95 por ciento para los 151 casos.



The Diagnosis of Morphologic Abnormalities of the Human Thyroid Gland by Means of I^{131}

FRANZ K. BAUER, M.D., WILLIAM E. GOODWIN, M.D., RAYMOND L. LIBBY, Ph.D.,
and BENEDICT CASSEN, Ph.D.

In previous reports (1, 2) a method of studying some of the morphological characteristics of the frontal profile of the human thyroid gland in its normal and abnormal states has been presented. The method uses I^{131} and the directional

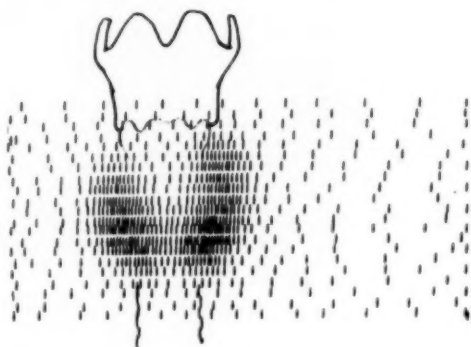


Fig. 1. Scintigram of a latex model of a normal human thyroid gland. The trachea and larynx are sketched in diagrammatically.

scintillation counter (3). The outline of the thyroid gland obtained by this method has been called a "scintigram."

It is the purpose of this paper to present the indications for this procedure and to demonstrate some illustrative cases.

METHOD

Briefly, the procedure of handling the patient is as follows: If visual outlining of the thyroid gland is recommended by the Hospital Radioisotope Committee, a dose of carrier-free I^{131} , ranging between 100 and 300 microcuries, is administered orally in capsule form (4). The exact dose used within this range depends upon the avidity of the thyroid gland for the isotope. It has been found desirable to have 60 to 80

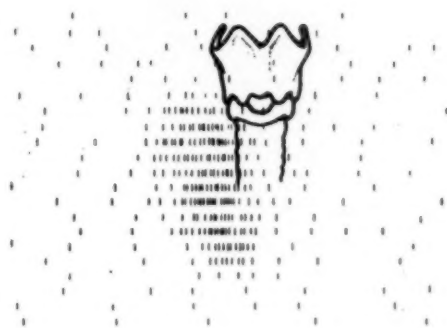


Fig. 2. Scintigram of "toxic" thyroid adenoma in a patient with hyperthyroidism. Note suppression of I^{131} accumulation in the remainder of the thyroid gland.

microcuries of I^{131} concentrated in the thyroid. The actual outlining procedure is done twenty-four or forty-eight hours after the dose of I^{131} has been administered; in hyperthyroid patients twenty-four hours is preferable. After the patient has been made comfortable, the scanning tube is run over the neck or any area in which functioning thyroid tissue is thought to be present. The scaling circuit of the instrument can be adjusted so that the printing relay will record every 2nd, 4th, 8th, 16th, 32nd, and 64th count. The choice of scale is such that areas containing I^{131} are recorded at about one millimeter centers, whereas over non-iodine accumulating areas the spacing is greater than this (Fig. 1).

INDICATIONS

Outlining the thyroid gland has become a routine clinical procedure in this hospital and is used in the following instances:

¹ From the Radioisotope Unit, Wadsworth General Hospital, Veterans Administration Center, Los Angeles, Calif., and the Departments of Medicine, Biophysics and Radiology, School of Medicine, University of California at Los Angeles. Presented at the Thirty-eighth Annual Meeting of the Radiological Society of North America, Cincinnati, Ohio, Dec. 7-12, 1952.

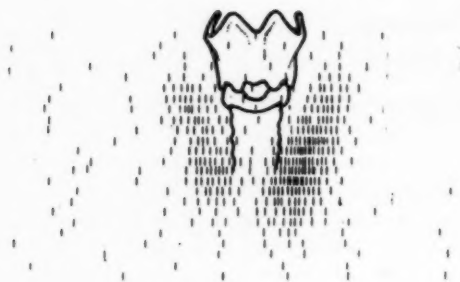


Fig. 3. Scintigram of thyroid shown in Fig. 2, six weeks after right hemithyroidectomy. Note remaining thyroid tissue in the right lobe and apparently normal function of the entire left lobe.

1. *Hyperthyroidism*: The question of a diffuse enlargement of "toxic" nodules cannot always be solved by palpation. It is well known that patients with "toxic" nodules who are clinically hyperthyroid may have normal I^{131} uptake values. "Toxic" nodules will appear as dense areas on the scintigram (Figs. 2 and 3), while the remainder of the thyroid gland is often not apparent because of suppression of function (5).

Diffusely enlarged glands (Fig. 4) are outlined by the procedure under discussion in order to estimate the correct weight of the gland by the formula of Allen and Goodwin (6). Recent observations on patients whose thyroid glands were obtained shortly after scintigrams had been made further confirmed the validity of the formula (7). Shrinkage of the diffusely enlarged gland following therapeutic doses of I^{131} can also be observed by means of this method (1).

Patients with recurrent hyperthyroidism following partial thyroidectomy are subjected to the outlining procedure in order to determine the amount of remaining gland tissue.

2. *Simple goiter*, including substernal extension of the thyroid gland.

3. *Solitary or multiple nodules*: Very often a solitary nodule (Fig. 5) is palpable but on the scintigram more than one "non-functioning" area can be demonstrated. Because of the belief that solitary nodules, particularly those which do not accumulate

I^{131} , i.e., "non-functioning," are more frequently associated with carcinoma of the thyroid, the visual demonstration of these nodules is extremely important.

4. *Carcinoma of the thyroid gland*: Only about one out of seven carcinomas of the thyroid gland is found to accumulate radioactive iodine. In these patients, not only primary lesions but also radioactive

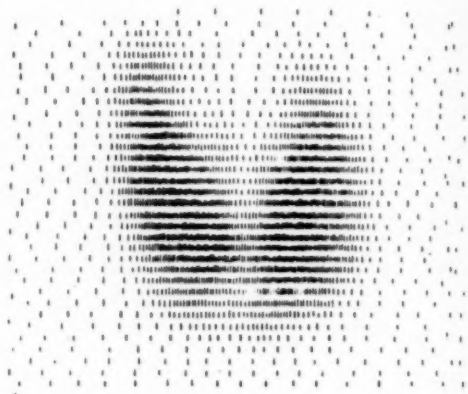


Fig. 4. Scintigram of a diffusely enlarged thyroid gland in a patient with hyperthyroidism.

iodine-accumulating metastases can be demonstrated by the scintigram. In those patients in whom carcinoma does not accumulate iodine, thyroidectomy will often make existing metastases concentrate radioactive iodine (8). Thiouracil and thyroid-stimulating hormone have also been used to enhance I^{131} accumulation in metastases from carcinoma of the thyroid (Fig. 6). In all these instances the outlining procedure is very helpful.

5. *Aberrant thyroid tissue* can be demonstrated by means of the scintigram.

COMMENT

It should be realized that the doses employed for this procedure are much higher than those used for diagnostic tracer studies in this laboratory, although they are comparable to the doses which had previously been considered in the tracer dose range and had frequently been used.

The directional scintillation counter used in this procedure has much greater collimation than the wide-angle counter which is used for diagnostic tracer studies (9). It records the activity of a very limited region, whereas the wide-angle counter records the activity of the entire thyroid gland. It is obvious from these considerations that the localizing (directional) scintillation counter requires the use of a



Fig. 5. Non-functioning area in the right lobe. Papillary carcinoma.

greater dose of I^{131} than that used for diagnostic tracer studies.

It should also be emphasized that at present the actual amount of I^{131} present in the gland cannot be determined from the scintigram. It is planned to correlate the visual profile of the gland (scintigram) with the actual amount of I^{131} present in it.

SUMMARY

A method using radioactive iodine for the visualization of the frontal profile of the thyroid gland is described. The indications for the procedure are discussed and illustrative cases are presented.

NOTE: The authors are indebted to Lucille E. Shoop, R.N., and Elsie M. Youtcheff, B.A., for their help in handling the patients and obtaining the scintigrams.

Veterans Administration Center
Los Angeles 25, Calif.

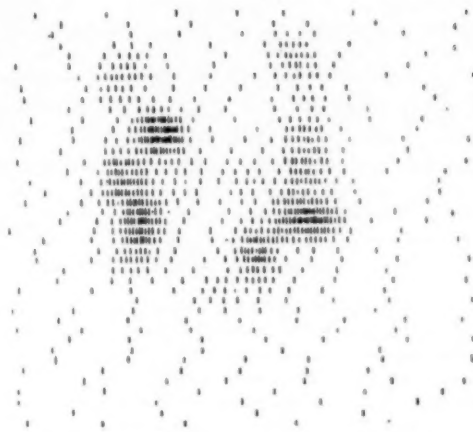


Fig. 6. Scintigram of a patient with carcinoma of the thyroid who had a total thyroidectomy. The metastases visible on the scintigram could be demonstrated only after thyrotrophic hormone stimulation. The patient had been given 200 millicuries of I^{131} over a period of a year before this scintigram was obtained. This eliminates the possibility of remaining normal thyroid tissue.

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(Para el sumario en español, véase la página siguiente.)

SUMARIO

El Diagnóstico de las Anomalías Morfológicas del Tiroides Humano por Medio del I¹³¹

El método descrito permite visualizar el perfil frontal del cuerpo tiroides usando yodo radioactivo y un cuentachispas encaminador. Usase para observar el hiper-

tiroidismo, el bocio simple, los nódulos solitarios o múltiples, el carcinoma y el tejido tiroideo aberrante. Muéstranse algunos casos típicos.

DISCUSSION

(Papers by Krohmer *et al.*, Andrews *et al.*, Bauer *et al.*, and Stirrett *et al.*)

Edith H. Quimby, Sc.D. (New York, N. Y.): On the first day of these meetings, a reporter came to talk to me about what might be said about hopeful things having to do with atomic energy. Could I tell him some of the things that would be useful to do. What I should have told him was: "Wait till Friday; come to the meeting."

There are a number of people who have voiced the opinion that, after all, isotopes aren't doing very much for us; we have had them for quite a while, and we are not getting forward very fast with them. I should like to remind you that radioactive isotopes were actually discovered less than twenty years ago, and have been widely available for only about five years. If we try to think where our science of radiology was from 1900 to 1905, perhaps it will give us some idea where we may hope to go with this branch of the science.

Actually, this group of papers we have heard today has been stimulating. It seems to me that anyone who heard them could never for a minute doubt that we have a great deal to look forward to both in diagnosis and therapy as far as radioactive isotopes are concerned.

To consider them separately: I have had no experience with the diagnosis of intraocular tumors on the basis that was recorded. This, of course, is not a new method. A long time ago Dr. Low-Beer recorded diagnoses of breast tumors by the same phosphorus uptake. This is not particularly a matter of increased uptake by intraocular tumors. Any rapidly growing tissue demonstrates increased uptake. Because radioactive phosphorus emits only beta rays, which can travel but a few millimeters in tissue, it is useful for superficial lesions.

The work just described would appear to be an extremely valuable adjunct to people who are studying diseases of the eye. It is not a difficult technic and I would think that many people would be interested in it. The dose of 500 microcuries is rather high; I would hope that some means might be discovered of lowering that, particularly if for any reason this test is going to be repeated.

With regard to radioactive gold, this is perhaps

one of the procedures whose curve of popularity has gone up very rapidly in the past year or year and a half. This must be because of the good results that are being achieved. In our institution, the radioactive gold program is administered in co-operation between the therapeutic radiologists and one particular surgeon, who has done all the follow-up on the patients. This surgeon expressed the opinion recently that radioactive gold is the greatest palliative agent he has encountered in the time he had been practicing medicine. I think this is an extremely important point. It sometimes seems that radiologists put too much stress on three-year cures or five-year cures, or something which they can call a cure, and forget that six months or eight months of comfortable life to the mother of a family, to a busy businessman, or to almost anybody, as far as that is concerned, is an extremely important thing. If, by this procedure, to patients who are in good health otherwise and need only to be relieved of fluid pressure, we can give comfortable life, that is certainly worth while. In our own institution, an evaluation of some 70 cases at the present time reveals that about 75 per cent of the intrapleural cases have been relieved, and something over 50 per cent of the intra-abdominal ones.

As to the scintigraph, I imagine that everybody in the audience, except the people who already own one, are envious. I am. I'd certainly like to have one. The sort of things that you can do with it are fascinating, as well as extremely useful. At the present time, the instrument is expensive, and many isotopists running on small budgets simply cannot afford one, particularly if the amount of thyroid work done is limited. But the thing to do is not to say, "Well, we can't do that, we haven't the machinery," for the necessary information can be obtained in selected cases, though more crudely and more slowly, by making carefully localized counts with a small end-window counter. This is being done by various procedures in various laboratories. Every laboratory which is doing much iodine work, I suspect, has some sort of a scanning arrangement which may be used when indicated.

One of the important things which has already

been said is that radioactive iodine tests are not a substitute for a clinical diagnosis. The scintigram and all the other tests, which the rest of us use, are not substitutes for clinical medicine, and never can be. There is always a danger, in the development of any diagnostic tool, that the medical man will lean too heavily upon it, and this, of course, has to be avoided. This is true whether it is one of the beautiful scintigraphs we have just seen, or a 24-hour iodine uptake, or anything in between, but it is also true that the information thus obtained is extremely useful to the clinician in making his diagnosis.

The liver study is completely new to me. I hadn't heard that it was being done, and it sounds extremely worth while. I am very anxious to get home and talk to some of the people there about it and see if they are not interested in trying it out in certain cases where it would seem to give extremely valuable information. It is a perfectly straightforward procedure, with a medium with which many of us are already familiar, with equipment most of us already have. I should think that probably a lot of the rest of you feel the way I do. Let's go home and try it.

I think this has been a wonderful program. I have been delighted to listen to it. I would like to express my own personal appreciation to every one of the speakers for a very interesting morning.

James Cook, M.D. (Detroit, Mich.): I wish first to express my appreciation for the privilege of discussing such a fine group of carefully prepared and scientifically sound presentations as we have had the pleasure of listening to this morning. I wish also to state that in my discussion I will base my remarks upon opinions prevailing in our own department at Harper Hospital, which are founded largely on work carried out by Dr. Kenneth Corrigan and his associates.

I was particularly interested in the paper on the detection of intraocular tumors by the use of radioactive phosphorus, inasmuch as we have pursued a similar study since the Spring of 1950. Our technic has been essentially the same except that we have not touched the eyeball and thus the eye was not necessarily anesthetized. It has been our feeling that the initial uptake shown by Mr. Krohmer and his associates is probably due to the increased vascularity of the tumor, and that the later uptake, appearing after forty-eight hours, is a more accurate measure of acceleration of activity of the tumor cells. For this reason we have made counts on the third and fifth days. In our experience inflammatory conditions give a faster initial uptake, and cases showing gross inflammatory changes, in our hands, have given questionable results. If, as indicated here today, there is a true index of malignancy illustrated by early increase in the

uptake of P^{32} by neoplastic tissue, we feel that it will greatly increase the clinical value of the method. There is always great demand for quick results in any diagnostic procedure, particularly when one deals with malignant disease. I might also add that in our diagnostic studies of intraocular tumors we have never used over 100 microcuries of radioactive phosphorus, and we also realize that by not touching the eyeball and by making our counts at greater distances with a thin aluminum filter we are actually counting the *Bremsstrahlung* rather than the beta particles from the P^{32} .

It is my feeling that this presentation is of value not only in bringing to the fore a diagnostic aid in the determination of intraocular tumors but also in suggesting that it may be possible to avail ourselves of this aid in a shorter time than has been heretofore thought possible.

The paper by Dr. Andrews and his associates concerning the use of intracavitary colloidal gold was truly enjoyed. The authors are to be complimented on bringing to our attention well observed cases in which radioactive colloidal gold has been used. We who have used it even sparingly have had reason to note its palliative possibilities, and it is through such carefully prepared presentations as this that we shall be able to find the niche that such substances will fill in future cancer therapy.

We, like other radiation therapists, have had a fair proportion of satisfactory palliative results in the treatment of pleural and peritoneal effusion by roentgen therapy. I realize that in this treatment we are also treating metastatic masses. Some of our more successful cases have been symptom- and fluid-free for as long as three years. Again trying to find that niche, and realizing that it is almost impossible to compare results of these two methods of treatment, would the authors care to give any indication of the time that the patients have been symptom-free as a result of treatment and would they wish to suggest the interval after which treatment might be repeated?

We have heard a very lucid description of some of the uses of the scintillation tube and it is interesting to see in these carefully prepared scintigrams, pictorial evidence of facts that have been established by accepted tracer technics for several years. It should, however, be observed that instruments that operate in only one plane have limitations in identifying thyroid distribution, and that a more flexible instrument, which can be used in three planes with the desired angulation and capable of responding to small changes in the patient's position, is often more effective. For example, it is sometimes profitable to use the patient's respiration in determining the depth of an intrathoracic tumor containing radioactive material. In this manner one can often

determine whether the tumor lies in the hilar nodes or is more closely incorporated into the less movable mediastinal area.

The value of the technic presented by Dr. Stirrett and his associates cannot be overemphasized. Any method which is helpful in determining the presence of liver metastases more accurately and earlier than is done by present means is welcome from the standpoint of evaluating the type of therapy to be used in caring for these patients as well as determining the prognosis, which is so often demanded from a tumor therapist. An over-all average of only 5 per cent error is certainly far better than can be obtained from any other known method of discovering metastatic involvement of the liver.

It might be noted that, in institutions without extensive electronic facilities, a simple well shielded and well constructed Geiger tube could be substituted for the more expensive scintillation counter. Such a tube gives more responsible results over a longer period of time. This has been demonstrated in the detection of brain tumors and similar localizations.

Herbert D. Kerman, M.D. (Louisville, Ky.): It has been a pleasure to hear this presentation this morning. In these papers two new possible diagnostic applications of radioisotopes have been presented.

From the very productive laboratory at Western Reserve another useful application of radiophosphorus has been carefully and critically evaluated. To possible localization of brain, breast, and testicular tumors, we can add intraocular lesions, further increasing the scope of diagnostic isotope studies. The provocative observation of the early rapid increase of activity in tumor tissue is extremely interesting. In other studies maximum counting rates have usually been obtained at the twenty-four-hour period or later. The possibilities of misinterpretation and the difficulties with deep lesions have been stressed, and the authors are to be commended for the conservatism of their analysis. It would seem, however, that complications of increased vascularity, edema, and inflammation might be limiting factors.

The report by Dr. Stirrett and his colleagues also opens a rather new avenue for diagnostic applications. Utilizing very highly collimated counters, we have found it perfectly possible to localize selectively small foci of increased activity of gallium 72 in phantom material containing fairly large concentrations of gallium. The problem in metastatic liver disease is finding a good gamma emitter which will localize selectively. Iodinated human serum albumin in brain tumors apparently crosses the blood-brain barrier and is thus localized in the tumor. Radiophosphorus has been shown to be incorporated in the in-

creased metabolic activity of neoplasms due to augmented synthesis within the cell of nucleic acids. We would like to ask Dr. Stirrett why labeled I*HSA is selectively taken up by metastatic liver tumors.

The scintigraph described by Dr. Bauer seems to be an ideal instrument for thyroid studies. We have followed the development of this instrument with considerable interest for some time and only regret the difficulties of obtaining good photomultiplier tubes and the expense of the equipment. The apparent convenience and accurate clinical usefulness of such an instrument cannot be denied and may outweigh these disadvantages. It would be a welcome instrument in any laboratory.

The use of radiogold as a palliative agent in the management of intractable effusions in cancer patients now appears to be a very reasonable method for control of this most distressing complication, and is being continued at several clinics. The experience generally has been that good results are obtained in approximately 30 to 50 per cent of patients and some benefit in another 10 to 15 per cent. Experience in other clinics has been that pleural effusions do somewhat better than peritoneal effusions, although our own experience is too limited to give any significant analysis of this. We believe the method to be safe, convenient, and well worth trial as a palliative procedure.

As an extension of this procedure, two other groups of patients may be considered as worthwhile candidates for this method of irradiation. Those patients who at surgery are found to have small peritoneal seedings without effusion, and those in whom spillage has occurred in an attempt to remove a malignant ovarian mass. The irradiation is probably effective to a depth of 3 mm., and radiogold administration might be used to control further spread or suppress further growth and fluid formation.

Marshall Brucer, M.D., Moderator: Dr. Andrews, you have been asked two questions: How long are patients symptom-free? Can the dosage be repeated?

Dr. Andrews: Most of our patients did not live more than one year after treatment, and most of them died from various manifestations of neoplasm. The longest improvement we have had is in a man with an undifferentiated carcinoma of the abdomen, primary site unknown. In this patient fluid appeared about two years ago and was treated about seventeen months ago; he has been clinically well without recurrence of fluid since then.

In regard to the problem of repetition of the treatment, we feel that it is worth-while in some cases to give more than one injection of the isotope. We usually wait at least six weeks or two

months after the initial treatment, partly in order to evaluate the effect, which may not be apparent before that length of time, and partly to observe the hematologic depression and to see whether the patient can tolerate further radiation. It appears that the limiting factor usually is not the hematologic depression but the degree of local fibrosis produced. This fibrosis may be particularly undesirable in patients treated by the intraperitoneal route. In the chest, it may be equally severe, but probably less likely to produce clinical symptoms. If two doses of the magnitude previously mentioned do not suffice to control the fluid, we would be inclined to believe that further treatment had little chance of success, but we would not arbitrarily limit the doses to two.

Dr. Brucer: Dr. Bauer, you are asked one question concerning the fact that this is a one-plane treatment only. Do you care to comment on that?

Dr. Bauer: It is a one-plane treatment, but we feel that, with one plane, we have got lots of information, more than we could get with manual counting. For many years Dr. Allen conducted a long series of tests with the manual directional counter. It took between two and three hours, and if the patient moved as much as a quarter of an inch, we were out. We sat there many, many afternoons to outline the gland. We feel that this new procedure, which takes five minutes, although it gives us only one plane, is more pleasant for the patient. There is nothing strapping him down. If he wants to scratch he can scratch, and we can start all over again.

As to the development of the system of three planes, we have tried it; we haven't been successful, and I don't know whether we have any reasonable hope of being able to do anything with it. As far as the thyroid is concerned, I don't know what we can do to improve it at the present time.

Dr. Brucer: Mr. Krohmer, the question has been raised as to the differentiation of tumors.

Mr. Krohmer: Dr. Kerman has asked if there isn't some limitation on differentiation. I believe that he means as a result of possible overlapping of the ratios for tumors and negatives. Am I right, Dr. Kerman? Is that what you have in mind? As yet, we haven't found that the ratios for tumors over which we can obtain direct measurements have overlapped the ratios for negatives, though certainly that possibility exists. With small tumors, it is quite possible that we could get lower ratios than we have for some of our negatives. We realize this. In the present results, however, the average of the ratios for the anterior tumors is about 1.8, with the lowest value being 1.4, and

for the negatives, all of which are anterior, the average ratio is 1.07 with the highest value 1.2. There is a definite gap between 1.2 and 1.4 for anterior conditions. I think that possibly it is fortuitous that we have such a gap. Actually, the posterior lesions fall into this gap, but there is good reason to believe that, if one obtains a higher ratio when the counter is not directly over the suspected tumor but only pointed toward it, the result has value. Our studies to date have shown this. I am quite certain that the limitation on differentiation does exist and will probably become evident as more patients are measured.

Dr. Brucer: Dr. Stirrett, you are asked a question as to radioassays of autopsy cases.

Dr. Stirrett: Radioassays were not done on autopsy cases, but in order to shed some light on the radiobiologic process involved in this procedure, liver biopsies were obtained at operation in several patients. A 300 microcurie dose of $I^{131}HSA$ was given twenty-four hours prior to operation, and biopsies were taken from the area of metastases and from an area of grossly normal liver. Radioassays revealed an average increase of 60 per cent in the area of metastases compared with the section of liver not involved by neoplasm.

Radioassays were also done on primary neoplasms obtained at operation. Sections were taken from the center of the tumor, from the margin, and from the adjacent normal tissue. It was observed that there was no significant difference in radioactivity in these sections except in those primary neoplasms which had undergone degeneration necrosis. In the tissue sections in which a reactive inflammatory and degenerative process was present, the radioactivity values were significantly higher than those obtained from normal tissue.

These observations lend support to the theory that in areas involved by metastatic neoplasm, there is an increased concentration of albumin as a result of an increased blood supply, edema, and necrosis. Other investigators have demonstrated that there is a disturbance in the albumin turnover in metastatic neoplasms resulting from damage to the capillary membrane.

Robert R. Newell, M.D. (San Francisco, Calif.): We have found that, if the end of the counter is directed obliquely in an attempt to measure further back than the conjunctival reflection, then the counts per second increase, even in a normal eye. This is because the window has been pulled away from contact. In the eye you have a unique situation. The vitreous is avascular and accumulates activity slowly. The choroid and retina become active promptly. When the counter is held with its window a few millimeters

from the sclera, some of the marginal choroid can deliver beta rays into the counter, rays which were cut off by the rim when it was in contact with the eyeball. Measurements in the first few minutes after injection, before the vitreous has come to equilibrium, can reveal themselves by the activity in the blood they hold, for they displace inactive vitreous.

Last week I tried to prove this notion in the laboratory. I made two bulbs with thin glass walls. One was simple; the other had a re-entrant bubble. Both were filled with P^{32} solution. When the counter was moved from contact to a few millimeters distance from the simple bulb, the counting rate fell off, as expected. But when this was tried with the thin sheet of P^{32} solution between the walls of the re-entrant bubble bulb, the counting rate increased with increasing separation for the first few millimeters, paradoxically.

Very early after injection, the counting rate over the tongue, for instance, falls off slowly as the counter is withdrawn a few millimeters from contact. But over the eyeball, the counting rate increases with the first few millimeters of separation. This anomaly fades out after ten minutes or so.

Counting rate is also increased on moving the window over an eye muscle, presumably because of its vascularity.

After hours or days, the activity becomes distributed in the several tissues in a wide range of concentrations. But excretion lowers the general level of activity so that counting becomes tedious and inaccurate.

We feel we have much more work to do to lay a firm foundation under this new diagnostic method.

Robert Loevinger, Ph.D. (New York, N. Y.): I would like to add a few words on the same subject. Several years ago we set out to investigate the use of surface activity measurements with P^{32} as a diagnostic tool. We, too, observed the very rapid rise in the first few seconds. In some cases, very close to a tumor, the rise is even more dramatic than shown by Mr. Krohmer. In the first minute, the count may be twenty times more over the tumor than over adjacent normal tissue. Over a fungating breast tumor or squamous-cell carcinoma of the cervix, the effect is very clear and very striking. There is, however, no diagnostic problem in such cases, and so no advantage in substituting a Geiger counter for a microscope. We abandoned the method, because in those cases where there was a diagnostic problem, a negative result could mean a tumor which is not malignant or one not superficial. One can never tell the amount of subcutaneous tissue that might be masking it. It did not occur to us to examine for intraocular tumors. That may be

just the useful case where the tumors are sufficiently superficial.

Surface counts show remarkable differences in different parts of the body. Over the sternum, the frontal area of the head, and the nipples, one gets a very rapid rise in surface activity after injection of P^{32} , something we cannot explain by vascularity. One must be very careful in choosing normal areas of the breast. If your Geiger counter includes part of the nipple on one side, but not on the other, you are not getting a true symmetrical, normal comparison.

Our work in general would support what has been reported by Krohmer, even though we made no measurements on the eye. Our work was done a few years ago and has been reported.

Bernard Roswit, M.D. (New York, N. Y.): At the Kingsbridge Veterans Hospital in the Bronx, we studied the *in vivo* uptake of P^{32} by testicular tumors in 40 patients, employing a 300 to 500 microcurie oral tracer dose and an end-window Geiger tube with mica window. Although a malignant neoplasm could be thus differentiated from a benign mass in a high percentage of the cases, active inflammatory lesions also demonstrated a high uptake of radiophosphorus. Deep-seated cancers (more than 6-8 mm.) and overlying edema often produced false negative readings. We wonder whether similar problems were encountered in ophthalmic tumors. Other radioisotopes are being investigated for preoperative diagnostic usefulness, for in suspected testicular cancer one dare not take a preoperative surgical biopsy.

Dr. Fields: I would like to ask Dr. Andrews if he has tried to use chromic phosphate for intracavitary injection. The half-value layer for Au^{199} is about 0.3 mm. and that for P^{32} would be close to 0.6 mm., and the added range might have some value.

Dr. Andrews: We haven't used chromic phosphate. We intend to do so. We think the greater penetration of the beta emission might be an improvement. We also think that the absence of the gamma emission might be an advantage in that there would be less total-body irradiation if the distribution of the chromic phosphate were the same as that of the gold.

Dr. Fields: We have used chromic phosphate in association with brain surgery in about 25 cases. The results are just beginning to be available. We have lost about 10 of these patients so far, but we believe that the treatment may have some value.

Question: With respect to radioactive gold, there is some suggestion in the literature that the treatment is more successful in patients with metastases of ovarian origin than in patients

with tumors from other primary sites. We have studied about 30 patients with intracavitary gold in the last year and we have gained the impression that those with lesions originating in the ovary have somewhat better results from the gold treatment. I wonder if Dr. Andrews would like to comment on that.

Dr. Andrews: As yet, we don't have any defi-

nite impression about the relationship of the site of the primary lesion, or of the histologic type, to the therapeutic results with intracavitary gold. The degree of dissemination of the tumor, the size of neoplastic masses, and the presence or absence of complications, such as intestinal obstruction and mediastinal compression, are the factors which seem to be important in determining the results in our patients.



Paraganglioma of the Stomach

A Case Report¹

HOWARD C. BURKHEAD, M.D., VERNER SWAN, M.D., and JOHN M. DORSEY, M.D.

WHILE NUMEROUS references to benign tumors of the stomach are to be found in the literature, a fairly careful search has revealed only one report of a gastric paraganglioma, that of Jones and McKee, in 1949. We present here the clinical history and operative findings in an additional case. Like Jones and McKee, we define

epigastric distress frequently followed by the passage of a tarry stool. Two days before admission there had been an attack of gastric discomfort, relieved by an antacid, but accompanied by a tarry stool. Severe hematemesis had occurred the following day, and again a tarry stool was passed.

Pertinent laboratory findings included a hemoglobin level of 11.5 gm. per 100 c.c. and a red cell count of 3,600,000.

X-ray examination of the stomach showed a filling

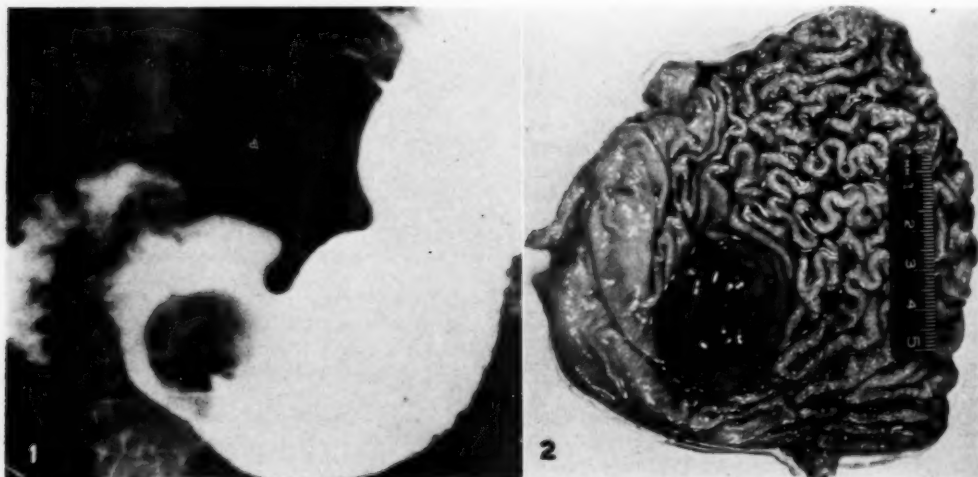


Fig. 1. Barium study of the stomach, showing rounded antral filling defect. On fluoroscopic examination peristaltic waves passed over the tumor, suggesting its benign nature.

Fig. 2. Photograph of the opened, resected gastric segment, in which can be seen the smooth rounded tumor.

paraganglioma as a chromaffin tumor occurring outside the adrenal as contrasted to a similar growth within the gland.

CASE REPORT

E. E., a white male executive, 50 years of age, was admitted to the Evanston Hospital on June 26, 1951, complaining of hematemesis and melena. For many years he had experienced intermittent episodes of dull pain in the left upper abdominal quadrant, lasting for approximately a week. The pain was not related to meals but was relieved by a bland diet. Ingestion of coarse foods produced

defect in the antrum, just proximal to the pylorus, measuring 4.0 cm. in diameter and smooth in outline (Fig. 1). This was believed to represent a tumor, while a second small defect near its base suggested an ulcer in the tumor. On fluoroscopic examination, the stomach appeared freely movable, with peristaltic waves passing over the tumor. A benign lesion, as a leiomyoma, aberrant pancreas, adenoma, or lipoma, was suspected.

On July 9, 1951, the abdomen was opened through an upper mid-line incision. On the anterior antral wall of the stomach were four masses of tissue, red to gray in color, 0.25 cm. in greatest diameter, growing through the gastric wall from the rounded intra-

¹ From the Evanston Hospital and Northwestern University Medical School (H. C. B., Resident in Radiology; V. S., Resident in Surgery; J. M. D., Chairman, Department of Surgery). Accepted for publication in November 1952.

gastric lesion. There was no adherence of this portion of the stomach to any surrounding tissue. Pieces of these tissues were sent to the laboratory for immediate frozen section and examination. Gastrotomy was done, and the gastric mucous membrane covering the rounded lesion in the gastric wall was divided, exposing a fairly firm, smooth, round granular tumor beneath. At one point there was an ulceration of the gastric mucous membrane, no doubt the source of the previous hemorrhage. Biopsy of this mass was done, and a tentative report of undifferentiated carcinoma was made. Consequently a gastrectomy with resection of the omentum and surrounding lymph nodes was performed. Recovery was uneventful.

The surgical specimen (Fig. 2) consisted of a segment of stomach measuring $11 \times 6 \times 3$ cm., with attached tissue of the greater and lesser omentum. In the greater curvature, 4.0 cm. from the distal line of resection, was a nodular tumor measuring 3.0 cm. in diameter. The overlying mucosa was intact, with the exception of a wedge-shaped defect resulting from excision of tissue for frozen-section biopsy. On cut section the tumor was well circumscribed, soft, gray, and slightly bulging. It completely replaced the muscularis and caused elevation of the mucosa and, to a slight degree, of the serosa.

Microscopic examination (Figs. 3 and 4) showed the overlying mucosa to be normal. The tumor cells

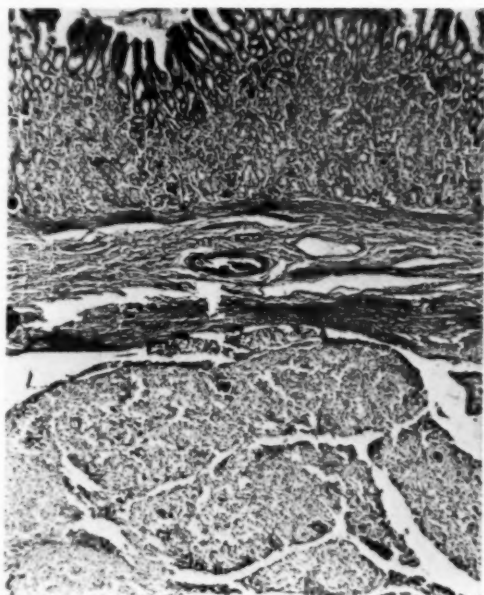


Fig. 3. Low-power microscopic view of a section taken through the tumor and the overlying gastric mucosal and submucosal layers. The absence of invasion is clearly seen.

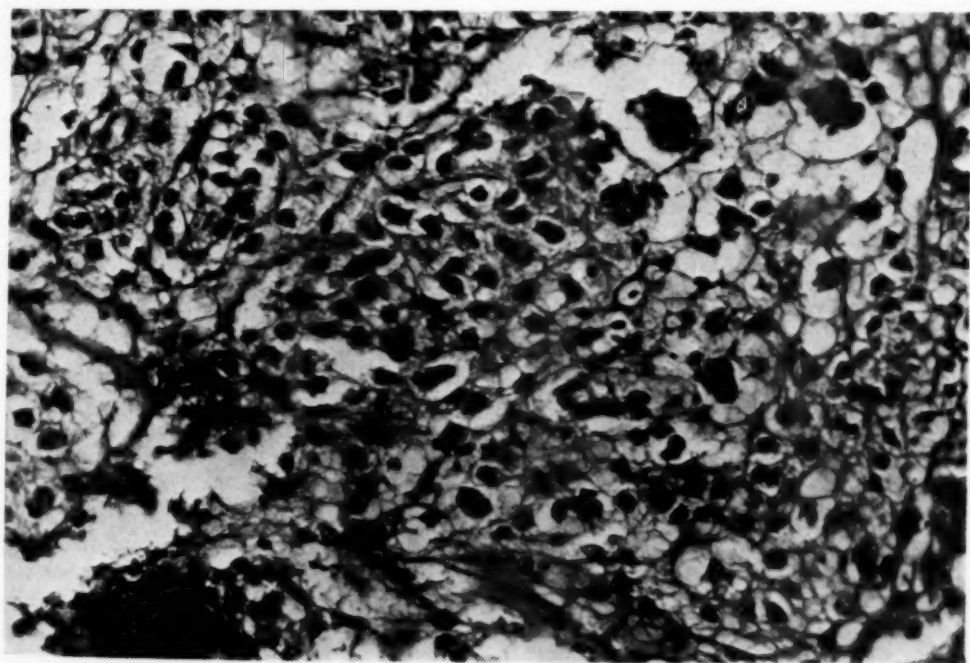


Fig. 4. Higher-power microscopic view through the tumor. For description, see text.

were arranged in nests, cords, and rosettes. They were moderate in size, slightly stellate in shape, poorly outlined, and had a finely granular, faintly basophilic cytoplasm. Vacuolation of the cytoplasm was prominent. The nuclei were small, slightly hyperchromatic, and for the most part regular in size. A few pleomorphic cells containing hyperchromatic nuclei were noted. No mitoses were seen. The stromal connective tissue was thin and scarce. Examination of slides stained by the McManus periodic acid method and by Foot and Foot's modification of Bielschowsky's silver impregnation method showed a fine reticulum of fibers which permeated the tumor and surrounded individual cellular elements. Thin-walled vascular spaces were present throughout; many spaces were lined with tumor cells. Sections of tissue fixed in chrome alum failed to reveal pigmentation of the tumor cells.

DISCUSSION

Jones and McKee's patient had postprandial discomfort for at least two years. He had one large rectal hemorrhage and

for two months previous to his admission had passed dark stools. Our case is similar. Symptoms and signs of benign gastric tumors can be quite suggestive, and the radiologist may be the first to suspect the diagnosis. Only by surgical biopsy, however, can one be certain of the nature of the lesion.

SUMMARY

A tumor of the stomach histologically resembling a paraganglioma is presented. The clinical course, x-ray appearance, gross appearance, and histologic picture are indicative of its benign character.

2650 Ridge Ave.
Evanston, Ill.

REFERENCE

JONES, C. K., AND MCKEE, F. W.: Gastric Paraganglioma with Ulceration. Report of Case. Arch. Path. 48: 570-577, December 1949.

SUMARIO

Paraganglioma del Estómago: Presentacion de un Caso

Descríbese aquí un caso de tumor gástrico extirpado quirúrgicamente, que histológicamente parecía ser paraganglioma. El caso es comparable al comunicado anteriormente por Jones y McKee, con historia de malestar gástrico, melena y hematemesis. El tumor aparecía en la radiografía como un nicho redondo en el antro del estómago. En el examen roentgenos-

cópico, observáronse ondas peristálticas que le pasaban por encima, sugiriendo así su naturaleza benigna.

Los síntomas y signos de los tumores gástricos benignos pueden ser muy indicativos, haciendo que el radiólogo sospeche el diagnóstico. Sin embargo, únicamente por medio de la biopsia es que puede establecerse la naturaleza del tumor.



EDITORIAL

Placentography

Hemorrhage secondary to placenta praevia is an alarming complication of pregnancy. It is therefore of great importance to the obstetrician to have exact knowledge of the position of the placenta so that appropriate measures may be taken to ward off impending danger. When it can be proved that placenta praevia is not present, conservative measures can be undertaken with the expectation of saving both the child and the mother. The roentgen examination has long since proved itself to be a safe and relatively accurate procedure and has contributed significantly to lowering the mortality rate incident to this complication.

During the past twenty-five years various roentgen methods have been developed to improve the accuracy of diagnosis of placenta praevia. It would seem appropriate to examine some of these and to analyze their safety factors and diagnostic usefulness. The methods chiefly calling for consideration are: (1) soft-tissue studies, (2) contrast studies of the bladder and rectum, (3) amniography, and (4) angiography.

Studies of the soft tissues for localization of the placenta cause the least discomfort and danger to the patient but demand an exacting technic. The placenta is usually seen as a kidney-shaped shadow of uniform density with its greater curvature following the uterine wall and its lesser curvature toward the fetus. Separating fetus and placenta is a dark line representing the more radiolucent fat of the fetal subcutaneous tissue. When the placenta occupies its normal position, this line begins in the fundus and may extend almost the full length of the fetus.

The appearance in placenta praevia was

recently described by Whitehead in the course of a symposium before the British Institute of Radiology. Lateral radiographs show the placental shadow low down in the general outline of the uterus. In cases of major degree the shadow may begin at about the middle of the uterus and spread down over the lower segment, making the diagnosis obvious. Many cases of lesser degree, however, do not present these typical appearances, and the placenta may appear to occupy a relatively normal position. It is then that other roentgen findings must be taken into account.

In the lateral view taken in the upright position, the location of the fetal head may give valuable information, especially in posterior placenta praevia. The placenta may be seen between the sacral promontory and the fetal head, which may be displaced anteriorly. Unfortunately, such displacement may be caused as well by tumors and certain deformities. In anterior placenta praevia, a similar visualization may be obtained, with displacement away from the symphysis pubis, but this is less reliable. Ball and Golden consider any displacement of the fetal head from the mid-line significant in films made in the standing position. They believe that placenta praevia can be definitely ruled out when the head is found dipping into the pelvic inlet and not displaced from the midcoronal or midsagittal plane.

Soft-tissue studies made with higher-voltage technic show promise of definite improvement in placental visualization.

Contrast studies by the use of cystography as a means of diagnosing placenta praevia were reported by Ude and Urner in 1935. They outlined the bladder by injecting

through a catheter about 40 c.c. of a 12.5 per cent solution of sodium iodide or other opaque material, with care not to produce over-distention. Normally the diameter of the soft tissues between the fetal head and the bladder lumen should be about 1 cm. Widening of this area indicates some abnormal interposed substance, usually placental tissue, though blood clots or some fetal abnormality may produce a similar picture. Cystography was used by Ude and Urner in 35 cases, of which 14 were diagnosed as placenta praevia. With a single exception, this diagnosis was subsequently confirmed.

Examination by this technic is of value in cephalic presentations only. It has subsequently been said to be reliable only if some part of the placenta is attached to the anterior wall of the lower segment, but the high incidence of success of the method would cast some doubt on this limitation. The method has been modified by the introduction of air into the bladder and into the rectum, as a contrast medium. It is thus possible to measure the thickness of the soft tissues between the fetal head and these organs. The air studies have proved to be of definite value, as an opaque medium sometimes obscures the margins of the fetal head.

Amniography consists in increasing the density of the amniotic fluid to give contrast to the fetal soft parts and the placenta. This procedure was originated in 1930 by Menees, Miller, and Holly, who injected strontium iodide through the anterior abdominal wall into the amniotic sac. They reported 21 cases without injurious results in normal pregnancies but with the induction of premature labor in one patient with placenta praevia. Reports, by various authors, of fetal deaths and the onset of premature labor have militated against general acceptance of the method.

In 1953 Savignac reviewed the literature on amniography and studied a small series of cases, using 70 per cent Diodrast as the preferred contrast material. He states that the procedure caused no untoward

results except in one case, in which injection was made into the placenta, causing a vasomotor reaction in the mother. He believes that the benefits from amniography are many: the placenta can be unerringly located; uterine tumors can be located and distinguished from the placenta; abnormalities of the fetus can be demonstrated; in multiple pregnancies the occurrence of a single or double placenta can be determined. Because a viable fetus will swallow the opacified material, failure to identify it in the fetal bowel is a valuable sign of fetal death. In some cases the maternal cystogram will reveal the relationship between the bladder and the fetal head.

Several studies have been reported on *arteriography* as a means of determining the position of the placenta. Norman injected Umbradil into the femoral artery in a retrograde direction, without producing any discernible fetal reaction or uterine contraction. In his technic the first film is taken just before the syringe has been completely emptied. Two seconds later a second film is taken, and the final film is obtained after another two seconds. In 15 cases of suspected placenta praevia an accurate opinion of the position of the placenta was formed in every case. In spite of the accuracy of the method, however, Norman and his associates use it only in strictly selected cases.

Another sign suggested by Norman is the soft blowing sound or *souffle*, heard on auscultation over the uterus. He believes that the position of the sound suggests the location of the placenta and that auscultation, with this in mind, may be a helpful method of supplementary study. The relationship between the path along which these sounds can be heard and the pattern of the vessels shown in the arteriogram, together with the position of the placenta as shown on the plain film, strongly suggests that the *souffle* originates in the widened uterine vessels supplying the placenta.

In any type of medical study, the method of examination must be balanced against

the gravity of the condition under investigation and safety of the patient. In placentography there is the additional danger to the child to be considered. The urgency of the situation, however, may sometimes be a compelling reason for adopting measures which carry a calculated risk. Some of the technics described above do carry this risk and should be resorted to only after simpler methods have failed to yield the desired information.

Soft-tissue studies without contrast media of any type are undoubtedly the safest method, providing judgment is used in the number of film exposures. This gives the general anatomical relationships of the maternal and fetal structures and in many instances visualizes the placenta. Studies following the introduction of a contrast medium into the bladder and rectum show a high degree of accuracy and appear to be entirely safe if proper technic is used. Amniography has received a considerable amount of criticism in the past, but with the newer technic may be develop-

ing along safer lines. Arteriography has been practiced to such a limited extent that opinions have not yet crystallized, but the users have adopted a cautious attitude. Injection of radioactive materials has been advocated by some, but the methods already described would appear to be safer.

A symposium entitled "Placentography" in the August 1953 issue of the *British Journal of Radiology* will be found to be profitable reading for those interested in this subject.

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ANNOUNCEMENTS AND BOOK REVIEWS

COLORADO RADIOLOGICAL SOCIETY

At the October meeting of the Colorado Radiological Society, Dr. William S. Curtis, of Boulder, was elected President; Dr. Raymond R. Lanier, of Denver, Vice-President; Dr. Thomas J. Kennedy, of Denver, Treasurer; Dr. Parker Allen, Children's Hospital, Denver, Secretary.

NORTH CAROLINA RADIOLOGICAL SOCIETY

Recently elected officers of the North Carolina Radiological Society are: President, Luther W. F. Oehlbeck, M.D., Morganton; President-Elect, Ivan E. Brouse, M.D., Wilmington; Vice-President, Thomas C. Worth, M.D., Raleigh; Secretary-Treasurer, W. C. Sternbergh, M.D., Charlotte Memorial Hospital, Charlotte. Dr. Robert J. Reeves, of Durham, is Councilor to the American College of Radiology.

RADIOLOGICAL SOCIETY OF SOUTHERN CALIFORNIA

The first meeting of the newly formed Radiological Society of Southern California was held at the Huntington Hotel, Pasadena, on Oct. 17, 1953.

Dr. Lyell C. Kinney of San Diego is the President of the Society, and Dr. Donald R. Laing of Pasadena the Secretary-Treasurer. Dr. James T. Case of Santa Barbara, Dr. Lowell S. Goin and Dr. John D. Camp of Los Angeles, along with the officers, constitute the Board of Directors.

TENNESSEE RADIOLOGICAL SOCIETY

Officers of the Tennessee Radiological Society for the current year are: Dr. Joseph McKinney Ivie, Nashville, President; Dr. J. Marsh Frère, Chattanooga, Vice-President; Dr. George K. Henshall, 311 Medical Arts Bldg., Chattanooga 3, Secretary-Treasurer.

EASTERN CONFERENCE OF RADIOLOGISTS

The Section on Radiology of the Medical Society of the District of Columbia will be host to the Eastern Conference of Radiologists at its 1954 session. The meeting will take place at the Statler Hotel, Washington, D. C., March 12 and 13, 1954. Registration will begin the afternoon of March 11.

The constituent organizations of the Conference are the New England Roentgen Ray Society, the New York Roentgen Ray Society, the Philadelphia Roentgen Ray Society, and the radiological sections of the Baltimore City Medical Society and of the District of Columbia Medical Society. The annual

session rotates among the five member groups.

An interesting program has been arranged, including a visit to the newly activated National Institutes of Health. Information may be obtained from Karl C. Corley, M.D., Chairman, Committee on Arrangements, 1835 Eye St., N. W., Washington 6, D. C.

DEUTSCHE RÖNTGEN-GESELLSCHAFT

At its Thirty-fifth Annual Meeting held recently in Stuttgart, the German Roentgen Society elected the following to honorary membership, in recognition of their significant contributions to radiology: Prof. W. Baensch, Washington; Prof. C. Gaiß, Bad Kissingen; Dr. med. h. c. B. Häuff, Stuttgart.

INTERNATIONAL SOCIETY OF RADIOLOGY

At the Seventh International Congress of Radiology held in Copenhagen during the past summer, it was voted to set up an International Society of Radiology, subject to the authority of the Congress, and the following were appointed to the Organizing Committee, with instructions to draw up a constitution for submission to the Eighth International Congress in 1956:

Prof. H. Holthusen, Germany, chairman; Ross Golden, M.D., United States; Prof. P. Flemming Møller, Denmark; Dr. Ralston Paterson, Great Britain; Dr. J. B. Pulcherio Filho, Brazil; and Prof. Flemming Nørgaard, Denmark, Honorary Secretary-Treasurer. Provisional headquarters of the society will be in Copenhagen.

The Congress voted to accept the invitation from Mexico to hold the Eighth Congress there. Prof. Manuel Madrazo was nominated President-elect.

DR. WILLIAM D. COOLIDGE HONORED

Four large units of the General Electric Company united to honor Dr. William D. Coolidge, former Vice-President and Director of Research for the Company, at a dinner in Cleveland, on his eightieth birthday, Oct. 20. Dr. Coolidge has many inventions to his credit but is probably best known for his development of ductile tungsten. His discoveries made possible the conversion of this tough metal into one of such pliability that it can be drawn into filaments only a fraction of the thickness of a human hair.

Books Received

Books received are acknowledged under this heading and such notice may be regarded as recognition of the courtesy of the sender. Reviews will be

published in the interest of our readers and as space permits.

MODERN TRENDS IN DIAGNOSTIC RADIOLOGY (Second Series). Edited by J. W. McLAREN, M.A., M.R.C.P., F.F.R., D.M.R.E., Radiologist, X-Ray Department, St. Thomas' Hospital, London; Sometime Examiner in Radiology, University of London. A volume of 413 pages, with 359 illustrations. Published by Paul B. Hoeber, Inc., Medical Book Department of Harper & Bros., New York, 1953. Price \$18.00.

RADIOACTIVE ISOTOPES: AN INTRODUCTION TO THEIR PREPARATION, MEASUREMENT AND USE. By W. J. WHITEHOUSE AND J. L. PUTMAN. A volume of 424 pages, with 155 illustrations. Published by Oxford University Press, New York, 1953. Price \$10.00.

Book Reviews

ADVANCES IN CANCER RESEARCH. Volume I. Edited by JESSE P. GREENSTEIN, National Cancer Institute, U. S. Public Health Service, Bethesda, Md., and ALEXANDER HADDOW, Chester Beatty Research Institute, Royal Cancer Hospital, London, England. A volume of 590 pages. Academic Press Inc., Publishers, New York, N. Y., 1953. Price \$12.00.

"Advances in Cancer Research" is the general title given to a projected series of volumes designed, according to the Editors, to reflect the "steady and inevitable march of the tides of our knowledge and increasing understanding" of an "ancient and elusive disease." This first volume is devoted largely to non-clinical phases of cancer research. As is to be expected, carcinogenesis comes in for a major share of attention, with chapters devoted to the development of epidermal cancer, the role of the milk agent in mammary cancer in mice, the hormonal aspects of experimental tumor genesis, and the carcinogenic aminoazo dyes. One chapter pertains to the application of radioisotopes to studies of carcinogenesis, and another to properties of the Rous chicken sarcoma agent. The last three chapters are of greater interest to the clinician. They deal with the chemistry of cytotoxic alkylating agents, nutrition in relation to cancer, and plasma proteins.

Each chapter of the book is written by a well known worker in the field covered, both American and British institutions being represented. Adequate bibliographies are included. Those interested in the

general aspects of cancer research will find here relatively full accounts of what is being done along a variety of lines.

MORRIS' HUMAN ANATOMY. A COMPLETE SYSTEMATIC TREATISE. Edited by J. PARSONS SCHAEFFER, A.M., M.D., Ph.D., Sc.D., D. Litt., Professor of Anatomy and Director of The Daniel Baugh Institute of Anatomy, Emeritus, The Jefferson Medical College. A volume of 1,718 pages, with 1,220 figures. Published by The Blakiston Co., New York, N. Y., Eleventh edition, 1953. Price \$16.00.

The first edition of *Morris' Human Anatomy* appeared in 1893 in London. The ten subsequent editions have all been published in the United States under the imprint of the present publisher. Over a span of sixty years the work has been accepted as a standard text on the most fundamental of the medical sciences, and there seems little doubt that it will continue to be so recognized.

The latest edition is edited by J. Parsons Schaeffer of Jefferson Medical College, and the contributors are all from institutions in the United States and Canada. With notable exceptions, the names are the same as those appearing in the Tenth Edition of 1942. New contributors are Prof. Ernest Lachman, of the University of Oklahoma, who has collaborated in the preparation of the section on The Digestive System; Prof. J. E. Markee, of Duke University, who is responsible for the section on the Urogenital System; Prof. C. G. Smith, of the University of Toronto, who assisted in revision of the section on The Musculature; and Prof. Mildred Trotter, of Washington University, who in association with Prof. Robert Terry revised the sections on Osteology and The Articulations.

Some sections of the work have been extensively rewritten, and all have been revised in the light of recent research. The book is abundantly illustrated in black and white and in color. An interesting feature for an anatomical text is the inclusion in the section on The Digestive System of a group of roentgenograms illustrating the appearance of the esophagus in relation to the aorta, variations in size, shape, and position of the stomach, and the appearances of the large and small intestines.

It goes without saying that a reliable treatise on anatomy is a must for every practitioner of medicine, whatever his special interest. Beginners and veteran physicians alike will find ample use for this familiar work in its latest form.

RADIOLOGICAL SOCIETIES: SECRETARIES AND MEETING DATES

Editor's Note: Secretaries of state and local radiological societies are requested to co-operate in keeping this section up-to-date by notifying the editor promptly of changes in officers and meeting dates.

RADIOLOGICAL SOCIETY OF NORTH AMERICA. *Secretary-Treasurer*, Donald S. Childs, M.D., 713 E. Genesee St., Syracuse 2, N. Y.

AMERICAN RADIUM SOCIETY. *Secretary*, Robert E. Fricke, M.D., Mayo Clinic, Rochester, Minn.

AMERICAN ROENTGEN RAY SOCIETY. *Secretary*, Barton R. Young, M.D., Germantown Hospital, Philadelphia 44, Penna.

AMERICAN COLLEGE OF RADIOLOGY. *Exec. Secretary*, William C. Stronach, 20 N. Wacker Dr., Chicago 6.

SECTION ON RADIOLOGY, A. M. A. *Secretary*, Paul C. Hodges, M.D., 950 East 59th St., Chicago 37.

Alabama

ALABAMA RADIOLOGICAL SOCIETY. *Secretary-Treasurer*, J. A. Meadows, Jr., M.D., Medical Arts Bldg., Birmingham 5.

Arizona

ARIZONA RADIOLOGICAL SOCIETY. *Secretary-Treasurer*, R. Lee Foster, M.D., 507 Professional Bldg., Phoenix. Annual meeting with State Medical Association; interim meeting in December.

Arkansas

ARKANSAS RADIOLOGICAL SOCIETY. *Secretary*, Fred Hames, M.D., Pine Bluff. Meets every three months and at meeting of State Medical Society.

California

CALIFORNIA MEDICAL ASSOCIATION, SECTION ON RADIOLOGY. *Secretary*, H. R. Morris, M.D., 1027 D St., San Bernardino.

EAST BAY ROENTGEN SOCIETY. *Secretary*, Dan Tucker, M.D., 434 30th St., Oakland 9. Meets monthly, first Thursday, at Peralta Hospital.

LOS ANGELES RADIOLOGICAL SOCIETY. *Secretary*, George Jacobson, M.D., 1200 North State St., Los Angeles 33. Meets monthly, second Wednesday, Los Angeles County Medical Association Bldg.

NORTHERN CALIFORNIA RADIOLOGICAL CLUB. *Secretary*, H. B. Stewart, Jr., M.D., 2920 Capitol Ave., Sacramento. Meets last Monday of each month, September to May.

PACIFIC ROENTGEN SOCIETY. *Secretary*, L. Henry Garland, M.D., 450 Sutter St., San Francisco 8. Meets annually at time of California State Medical Association convention.

RADIOLOGICAL SOCIETY OF SOUTHERN CALIFORNIA. *Secretary-Treasurer*, Donald R. Laing, M.D., 65 North Madison Ave., Pasadena 1.

SAN DIEGO RADIOLOGICAL SOCIETY. *Secretary*, C. W. Bruner, M.D., 2456 Fourth Ave., San Diego 1. Meets first Wednesday of each month.

SAN FRANCISCO RADIOLOGICAL SOCIETY. *Secretary*, I. J. Miller, M.D., 2680 Ocean Ave., San Francisco 27. Meets quarterly, at the University Club.

SOUTH BAY RADIOLOGICAL SOCIETY. *Secretary*, William H. Graham, M.D., 634 E. Santa Clara St., San Jose 12. Meets monthly, second Wednesday.

X-RAY STUDY CLUB OF SAN FRANCISCO. *Secretary*, Wm. W. Saunders, M.D., VA Hospital, San Francisco 21. Meets third Thursday at 7:45, Lane Hall, Stanford University Hospital.

Colorado

COLORADO RADIOLOGICAL SOCIETY. *Secretary*, Parker Allen, M.D., Children's Hospital, Denver. Meets monthly, third Friday, at University of Colorado Medical Center or Denver Athletic Club.

Connecticut

CONNECTICUT STATE MEDICAL SOCIETY, SECTION ON RADIOLOGY. *Secretary-Treasurer*, William A. Goodrich, M.D., 85 Jefferson St., Hartford 14. Meets bimonthly, second Wednesday.

CONNECTICUT VALLEY RADIOLOGICAL SOCIETY. *Secretary*, B. Bruce Alicandri, M.D., 20 Maple St., Springfield, Mass. Meets second Friday of October and April.

District of Columbia

RADIOLOGICAL SECTION, DISTRICT OF COLUMBIA MEDICAL SOCIETY. *Secretary*, Alvin C. Wyman, M.D., 5445 28th St., N.W., Washington. Meets third Wednesday, January, March, May, and October, at 8:00 P.M., in Medical Society Library.

Florida

FLORIDA RADIOLOGICAL SOCIETY. *Secretary-Treasurer*, Hugh G. Reaves, M.D., Medical Arts Bldg., Sarasota. Meets in April and in October.

GREATER MIAMI RADIOLOGICAL SOCIETY. *Secretary*, E. Hampton Bryson, M.D., 273 Alhambra Circle, Coral Gables. Meets monthly, third Wednesday, 8:00 P.M., Veterans Administration Bldg., Miami.

Georgia

ATLANTA RADIOLOGICAL SOCIETY. *Secretary-Treasurer*, Albert A. Rayle, Jr., M.D., 490 Peachtree St. Meets second Friday, September to May.

GEORGIA RADIOLOGICAL SOCIETY. *Secretary-Treasurer*, Robert M. Tankesley, M.D., 218 Doctors Bldg., Atlanta. Meets in November and at the annual meeting of the State Medical Association.

RICHMOND COUNTY RADIOLOGICAL SOCIETY. *Secretary*, Wm. F. Hamilton Jr., M.D., University Hospital, Augusta.

Hawaii

RADIOLOGICAL SOCIETY OF HAWAII. *Secretary*, Philip S. Arthur, M.D., Suite 42, Young Hotel Bldg., Honolulu. Meets third Friday of each month.

Illinois

CHICAGO ROENTGEN SOCIETY. *Secretary*, Elbert K. Lewis, M.D., 6337 S. Harvard Ave., Chicago 21. Meets at the University Club, second Thursday of October, November, January, February, March, and April at 8:00 P.M.

ILLINOIS RADIOLOGICAL SOCIETY. *Secretary-Treasurer*, Stephen L. Casper, M.D., Physicians and Surgeons Clinic, Quincy.

ILLINOIS STATE MEDICAL SOCIETY, SECTION ON RADIOLOGY. *Secretary*, George E. Irwin, Jr., M.D., 427 N. Main St., Bloomington.

Indiana

INDIANA ROENTGEN SOCIETY. *Secretary-Treasurer*, John A. Robb, M.D., 23 East Ohio St., Indianapolis. Annual meeting in May.

Iowa

IOWA RADIOLOGICAL SOCIETY. *Secretary*, James T. McMillan, M.D., 1104 Bankers Trust Bldg., Des Moines. Meets during annual session of State Medical Society, and holds a scientific session in the Fall.

Kansas

KANSAS RADIOLOGICAL SOCIETY. *Secretary*, Willis L. Beller, M.D., 700 Kansas Ave., Topeka. Meets in the Spring with the State Medical Society and in the Winter on call.

Kentucky

KENTUCKY RADIOLOGICAL SOCIETY. *Secretary*, Everett L. Pirkey, M.D., Louisville General Hospital. Meets monthly, second Friday, at Seelbach Hotel, Louisville.

Louisiana

ORLEANS PARISH RADIOLOGICAL SOCIETY. *Secretary*, Joseph V. Schlosser, M.D., Charity Hospital of Louisiana, New Orleans 13. Meets second Tuesday of each month.

RADIOLOGICAL SOCIETY OF LOUISIANA. *Secretary-Treasurer*, J. T. Brierre, M.D., 700 Audubon Bldg., New Orleans.

SHREVEPORT RADIOLOGICAL CLUB. *Secretary*, W. R. Harwell, M.D., 608 Travis St. Meets monthly September to May, third Wednesday.

Maine

MAINE RADIOLOGICAL SOCIETY. *Secretary-Treasurer*, Hugh Allan Smith, M.D., Eastern Maine General Hospital, Bangor. Meets three times a year—Spring, Summer, and Fall.

Maryland

BALTIMORE CITY MEDICAL SOCIETY, RADIOLOGICAL SECTION. *Secretary-Treasurer*, H. Leonard Warres, M.D., 2337 Eutaw Place, Baltimore 17. Meets third Tuesday, September to May.

MARYLAND RADIOLOGICAL SOCIETY. *Secretary-Treasurer*, H. Leonard Warres, M.D., 2337 Eutaw Place, Baltimore 17.

Michigan

DETROIT X-RAY AND RADIUM SOCIETY. *Secretary*, E. F. Lang, M.D., Harper Hospital, Detroit 1. Meets first Thursday, October to May, at Wayne County Medical Society club rooms.

Minnesota

MINNESOTA RADIOLOGICAL SOCIETY. *Secretary*, John R. Hodgson, M.D., The Mayo Clinic, Rochester. Meets in Spring and Fall.

Mississippi

MISSISSIPPI RADIOLOGICAL SOCIETY. *Secretary-Treasurer*, John W. Evans, M.D., 117 N. President St., Jackson, Miss. Meets monthly, third Tuesday, at 6:30 P.M., at the Rotisserie Restaurant, Jackson.

Missouri

RADIOLOGICAL SOCIETY OF GREATER KANSAS CITY. *Secretary*, James E. McConchie, M.D., First National Bank Bldg., Independence, Mo. Meets last Friday of each month.

ST. LOUIS SOCIETY OF RADIOLOGISTS. *Secretary*, Francis O. Trotter, Jr., M.D., 634 North Grand Blvd. Meets on fourth Wednesday, October to May.

Montana

MONTANA RADIOLOGICAL SOCIETY. *Secretary*, Grant P. Raitt, M.D., 413 Medical Arts Bldg., Billings. Meets annually.

Nebraska

NEBRASKA RADIOLOGICAL SOCIETY. *Secretary-Treasurer*, James F. Kelly, Jr., M.D., 816 Medical Arts Bldg., Omaha. Meets third Wednesday of each month at 6 P.M. in Omaha or Lincoln.

New England

NEW ENGLAND ROENTGEN RAY SOCIETY. *Secretary*, Stanley M. Wyman, M.D., Massachusetts General Hospital, Boston 14. Meets monthly on third Friday, at the Harvard Club, Boston.

New Hampshire

NEW HAMPSHIRE ROENTGEN SOCIETY. *Secretary*, Albert C. Johnston, M.D., 127 Washington St., Keene.

New Jersey

RADIOLOGICAL SOCIETY OF NEW JERSEY. *Secretary*, Salomon Silvera, M.D., 921 Bergen Ave., Jersey City. Meets at Atlantic City at time of State Medical Society and midwinter in Elizabeth.

New York

BUFFALO RADIOLOGICAL SOCIETY. *Secretary-Treasurer*, Mario C. Gian, M.D., 610 Niagara St., Buffalo 1. Meets second Monday, October to May.

CENTRAL NEW YORK ROENTGEN SOCIETY. *Secretary*, Dwight V. Needham, M.D., 608 E. Genesee St., Syracuse 2. Meets in January, May, and October.

KINGS COUNTY RADIOLOGICAL SOCIETY. *Secretary,* Solomon Maranov, M.D., 1450 51st St., Brooklyn 19. Meets fourth Thursday, October to April (except December), at 9:00 P.M., Kings County Medical Bldg.

NASSAU RADIOLOGICAL SOCIETY. *Secretary,* Frank Huber, M.D., 131 Fulton Ave., Hempstead, N. Y. Meets second Tuesday, February, April, June, October, and December.

NEW YORK ROENTGEN SOCIETY. *Secretary,* Jacob R. Freid, M.D., 1049 Park Ave., New York.

NORTHEASTERN NEW YORK RADIOLOGICAL SOCIETY. *Secretary-Treasurer,* Donald H. Baxter, M.D., Albany Hospital, Albany. Meets in the capital area second Wednesday, October, November, March, and April. Annual meeting in May or June.

RADIOLOGICAL SOCIETY OF NEW YORK STATE. *Secretary-Treasurer,* Mario C. Gian, M.D., 610 Niagara St., Buffalo. Meets annually with the State Medical Society.

ROCHESTER ROENTGEN-RAY SOCIETY. *Secretary-Treasurer,* A. Gordon Ide, M.D., 277 Alexander St. Meets at Strong Memorial Hospital, 8:15 P.M., last Monday of each month, September through May.

WESTCHESTER RADIOLOGICAL SOCIETY. *Secretary,* Charles G. Huntington, M.D., 170 Maple Ave., White Plains, N. Y. Meets third Tuesday of January and October and at other times as announced.

North Carolina

RADIOLOGICAL SOCIETY OF NORTH CAROLINA. *Secretary,* Waldemar C. A. Sternbergh, M.D., 1400 Scott Ave., Charlotte 2. Meets in April and October.

North Dakota

NORTH DAKOTA RADIOLOGICAL SOCIETY. *Secretary-Treasurer,* H. Milton Berg, M.D., Quain & Ramstad Clinic, Bismarck. Meets in the Spring with State Medical Association; in Fall or Winter on call.

Ohio

OHIO STATE RADIOLOGICAL SOCIETY. *Secretary-Treasurer,* M. M. Thompson, Jr., M.D., 316 Michigan St., Toledo. Meets with State Medical Association.

CENTRAL OHIO RADIOLOGICAL SOCIETY. *Secretary,* Frank A. Riebel, M.D., 15 W. Goodale St., Columbus. Meets second Thursday, October, December, February, April, and June, 6:30 P.M., Columbus Athletic Club, Columbus.

CLEVELAND RADIOLOGICAL SOCIETY. *Secretary-Treasurer,* Mortimer Lubert, M.D., Heights Medical Center Bldg., Cleveland Heights 6. Meets at 6:45 P.M. on fourth Monday, October to April, inclusive.

GREATER CINCINNATI RADIOLOGICAL SOCIETY. *Secretary-Treasurer,* Chapin Hawley, M.D., 927 Carew Tower, Cincinnati 2. Meets first Monday of each month, September to June, at Cincinnati General Hospital.

MIAMI VALLEY RADIOLOGICAL SOCIETY. *Secretary,* W. S. Koller, M.D., 60 Wyoming St., Dayton. Meets monthly, second Friday

Oklahoma

OKLAHOMA STATE RADIOLOGICAL SOCIETY. *Secretary-Treasurer,* John R. Danstrom, M.D., Medical Arts Bldg., Oklahoma City.

Oregon

OREGON RADIOLOGICAL SOCIETY. *Secretary-Treasurer,* John Wayne Loomis, M.D., 919 Taylor Street Bldg., Portland 5. Meets monthly, second Wednesday, October to June, at 8:00 P.M., University Club, Portland.

Pacific Northwest

PACIFIC NORTHWEST RADIOLOGICAL SOCIETY. *Secretary-Treasurer,* Sydney J. Hawley, M.D., 1320 Madison St., Seattle 4. Meets annually in May.

Pennsylvania

PENNSYLVANIA RADIOLOGICAL SOCIETY. *Secretary-Treasurer,* James M. Converse, M.D., 416 Pine St., Williamsport 8. Meets annually.

PHILADELPHIA ROENTGEN RAY SOCIETY. *Secretary,* Herbert M. Stauffer, M.D., Temple University Hospital, Philadelphia 40. Meets first Thursday of each month at 5:00 P.M., from October to May, in Thompson Hall, College of Physicians.

PITTSBURGH ROENTGEN SOCIETY. *Secretary-Treasurer,* Donald H. Rice, M.D., 4800 Friendship Ave., Pittsburgh 24. Meets monthly, second Wednesday, at 6:30 P.M., October to May, at Webster Hall.

Rocky Mountain States

ROCKY MOUNTAIN RADIOLOGICAL SOCIETY. *Secretary-Treasurer,* John H. Freed, M.D., 4200 East Ninth Ave., Denver 7, Colo.

South Carolina

SOUTH CAROLINA RADIOLOGICAL SOCIETY. *Secretary-Treasurer,* William A. Klauber, M.D., Self Memorial Hospital, Greenwood. Meets with State Medical Association in May.

South Dakota

RADIOLOGICAL SOCIETY OF SOUTH DAKOTA. *Secretary-Treasurer,* Donald J. Peik, M.D., 303 S. Minnesota Ave., Sioux Falls. Meets during annual meeting of State Medical Society.

Tennessee

MEMPHIS ROENTGEN CLUB. *Secretary,* Harvey Thompson, M.D., 899 Madison Ave. Meets first Monday of each month at John Gaston Hospital.

TENNESSEE RADIOLOGICAL SOCIETY. *Secretary-Treasurer,* George K. Henshall, M.D., 311 Medical Arts Bldg., Chattanooga 3. Meets annually with State Medical Society in April.

Texas

DALLAS-FORT WORTH ROENTGEN STUDY CLUB. *Secretary,* Claude Williams, M.D., Fort Worth. Meets monthly, third Monday, in Dallas odd months, Fort Worth even months.

HOUSTON RADIOLOGICAL SOCIETY. *Secretary,* Harry Fishbein, M.D., 324 Medical Arts Bldg., Houston 2.

SAN ANTONIO-MILITARY RADIOLOGICAL SOCIETY. *Secretary*, Hugo F. Elmendorf, Jr., M.D., 730 Medical Arts Building, San Antonio 5, Texas. Meets at Brook Army Medical Center, the first Monday of each month.

TEXAS RADIOLOGICAL SOCIETY. *Secretary-Treasurer*, R. P. O'Bannon, M.D., 650 Fifth Ave., Fort Worth. Next meeting Jan. 29-30, 1954, Dallas.

Utah

UTAH STATE RADIOLOGICAL SOCIETY. *Secretary-Treasurer*, Angus K. Wilson, M.D., 343 S. Main St., Salt Lake City 1. Meets third Wednesday, January, March, May, September, November.

Virginia

VIRGINIA RADIOLOGICAL SOCIETY. *Secretary*, P. B. Parsons, M.D., 1308 Manteo St., Norfolk 7.

Washington

WASHINGTON STATE RADIOLOGICAL SOCIETY. *Secretary-Treasurer*, John N. Burkey, M.D., 555 Medical-Dental Bldg., Seattle. Meets fourth Monday, September through May, at College Club, Seattle.

West Virginia

WEST VIRGINIA RADIOLOGICAL SOCIETY. *Secretary*, W. Paul Elkin, 515-519, Medical Arts Bldg., Charleston. Meets concurrently with annual meeting of State Medical Society, and at other times as arranged by Program Committee.

Wisconsin

MILWAUKEE ROENTGEN RAY SOCIETY. *Secretary-Treasurer*, Jerome L. Marks, M.D., 161 W. Wisconsin Ave., Milwaukee 1. Meets monthly on fourth Monday at the University Club.

SECTION ON RADIOLOGY, STATE MEDICAL SOCIETY OF WISCONSIN. *Secretary*, Abraham Melamed, M.D., 425 E. Wisconsin Ave., Milwaukee 2. Meets in October with State Medical Society.

UNIVERSITY OF WISCONSIN RADIOLOGICAL CONFERENCE. Meets first and third Thursday at 4 P.M., September to May, Service Memorial Institute.

WISCONSIN RADIOLOGICAL SOCIETY. *Secretary-Treasurer*, W. W. Moir, M.D., Sheboygan Memorial Hospital, Sheboygan.

Puerto Rico

ASOCIACIÓN PUERTORRIQUEÑA DE RADIOLOGÍA. *Secretary*, Rafael A. Blanes, M.D., Box 9724 Santurce, Puerto Rico.

CANADA

CANADIAN ASSOCIATION OF RADIOLOGISTS. *Honorary Secretary-Treasurer*, D. L. McRae, M.D. *Asso-Hon. Secretary-Treasurer*, Guillaume Gill, M.D. *Central Office*, 1555 Summerhill Ave., Montreal 25, Quebec. Meets in January and June.

LA SOCIÉTÉ CANADIENNE-FRANÇAISE D'ELECTROLOGIE ET DE RADIOLOGIE MÉDICALES. *General Secretary*, Origène Dufresne, M.D., Institut du Radium, Montreal. Meets third Saturday of each month.

CUBA

SOCIEDAD DE RADIOLOGÍA Y FISIOTERAPIA DE CUBA. *Secretary*, Dr. Rafael Gómez Zaldivar. Offices in Hospital Mercedes, Havana. Meets monthly.

MEXICO

SOCIEDAD MEXICANA DE RADIOLOGÍA Y FISIOTERAPIA. *General Secretary*, Dr. Dionisio Pérez Cosío, Marsella 11, Mexico, D.F. Meets first Monday of each month.

PANAMA

SOCIEDAD RADIOLÓGICA PANAMEÑA. *Secretary-Editor*, Luis Arrieta Sánchez, M.D., Apartado No. 86, Panama, R. de P.



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ROENTGEN DIAGNOSIS

THE HEAD AND NECK

The Roentgenologic Appearance of the Aqueduct of Sylvius. E. Lindgren and G. di Chiro. *Acta radiol.* 39: 117-125, February 1953.

The normal aqueduct of Sylvius appears in lateral encephalograms as a narrow channel connecting the third and fourth ventricles. In a series of 300 encephalograms performed in the Roentgen Department of Serafimerlasarettet, Stockholm, the course was found to vary. In about 35 per cent it was smoothly curved from the posterior lower part of the third ventricle to the fourth ventricle. In the majority of cases (65 per cent), however, it formed various angles, the anterior portion coursing horizontally while the posterior portion curved sharply downward, becoming almost vertical. The aqueduct reaches as far as the quadrigeminal plate, which forms its upper dorsal border. The angle seems to correspond to the border between the superior and inferior colliculi. There is often a kink in the normal aqueduct. This is usually not pronounced but occasionally, when it is marked, the appearance may closely resemble that produced by an expanding lesion of the posterior fossa.

The exact length of the aqueduct has not been satisfactorily determined. It has previously been given as anywhere from 1.5 to 3 cm. According to careful measurements by the authors in 30 cases, it was nearly constant between 1.6 and 1.8 cm. The landmarks for the measurements may, of course, vary, and it is likely that the previous greater measurements included part of the fourth ventricle.

The shape of the aqueduct seems to depend primarily on the anatomic shape and position of the quadrigeminal plate, which is resistant to pressure. Expanding lesions behind and beneath the quadrigeminal plate will cause the aqueduct to become kinked at its weakest point, which is the border between the superior and inferior colliculi. In expanding lesions so situated that they cause only a widening of the fourth ventricle, the plate turns backward and upward, in its entirety, and as a result the aqueduct is dilated. Expanding lesions situated behind and above the quadrigeminal plate will tip the plate forward. Tumors of the quadrigeminal plate itself are very rare but in their presence the border of the aqueduct becomes irregular and there is likely to be a change in the appearance of the dorsal part of the third ventricle.

Seven roentgenograms; 5 photographs; 1 graph.

JOHN F. RIESSER, M.D.
Springfield, Ohio

A Comparative Study of the Use of Diiodofluorescein and Iodinated Human Serum Albumin for the Diagnosis and Localization of Intracranial Neoplasms. Eric T. Yuhl, Lloyd A. Stirrett, and Raymond L. Libby. *Ann. Surg.* 137: 184-188, February 1953.

The initial successful external localizations of brain tumors by radiotracer technics were accomplished with radioactive diiodofluorescein as the tracer. Later, iodinated human serum albumin was used as the tracer material and the scintillation counter replaced the Geiger-Müller counter. The authors describe in detail their methods in the use of both tracers in the localization of intracranial neoplasms.

Diiodofluorescein was used in surveying 24 patients

suspected of having intracranial tumors; 17 of these were subsequently found not to have a neoplasm, while 7 had brain tumors proved at surgery. In this group of 24 cases, 2 false positive and 2 false negative diagnoses were made by the isotope studies. The diagnostic accuracy was recorded as 83 per cent.

Iodinated human serum albumin was used as the tracer in 20 patients suspected of having intracranial neoplasms. Craniotomy and biopsy disclosed a tumor in 9 of these individuals. Two false positive diagnoses were made by the isotope method, and a diagnostic accuracy of 90 per cent was recorded for the group.

The experiences of the authors lead them to believe that iodinated human serum albumin offers several advantages for the study of intracranial lesions. Smaller amounts give a higher counting rate than diiodofluorescein. Also, the rate of excretion is slower, thus giving the examiner more time in which to complete the examination. A disadvantage of diiodofluorescein is its rapid concentration in the liver, producing a right-sided asymmetrical radioactive source which may interfere with the reliability of the test. Finally, the iodinated serum albumin has a greater differential concentration in the abnormal area than diiodofluorescein, which would probably explain the more precise focal localization obtained with the former. In the observations recorded here, the radioactivity survey with diiodofluorescein did not precisely localize any of the 7 verified neoplasms. In 6 of the 9 verified cases in the iodinated serum albumin series, exact localization was obtained.

Two photographs; 2 tables.

DEAN W. GEHEBER, M.D.
Baton Rouge, La.

Recent Advances in the Diagnosis and Treatment of Cerebral Vascular Accidents. Exum Walker, William W. Moore, James R. Simpson, and F. Vatnar Kristoff. *South. M. J.* 46: 136-143, February 1953.

A brief discussion of the various intracranial vascular lesions is presented, including some of the differential diagnoses to be considered. The roentgenographic and therapeutic aspects of the following conditions are briefly considered: intracerebral hemorrhage, cerebral thrombosis, subarachnoid hemorrhage, arteriovenous fistula, embolism, brain tumor, and chronic subdural hematomas. Twenty-six reproductions of radiographs illustrate the various lesions. No series of cases and no statistics are presented.

The authors emphasize that in recent years the diagnosis of the exact nature of the various cerebral vascular accidents has become increasingly more accurate. With this advance, the treatment of these lesions can be much more definitive. No longer should physicians be satisfied with the general diagnosis of "stroke."

JOHN M. KOHL, M.D.
Jefferson Medical College

High-Voltage Technic and Fine-Focus Tube in Roentgenography of the Larynx. Detlev Schoen. *Fortschr. a. d. Geb. d. Röntgenstrahlen* 78: 170-173, February 1953 (In German)

The author advises high voltage (125 kv.) and a fine-focus tube for radiologic examination of the larynx. With high voltage, the contrast of the superimposed

bony parts will be diminished and therefore the details of the larynx, as the sinus Morgagni, and neighboring soft parts will be better visualized. The exposure must be made during phonation. The vocal "u" (conforming to "oo," as in wood, in English) is the best sound. Films obtained with this technic usually are diagnostic. Tomography continues, however, to be the most precise method.

Five roentgenograms; 2 schematic drawings.

LEWIS L. HAAS, M.D.
Chicago, Ill.

Stroke Resulting from Internal Carotid Artery Thrombosis in the Neck. E. S. Gurdjian and J. E. Webster. *J.A.M.A.* 151: 541-545, Feb. 14, 1953.

The authors review the literature on internal carotid artery thrombosis and summarize their own experience with 30 patients. The signs and symptoms may be of sudden onset or the course may be slowly progressive. Hemiplegia or hemiparesis coming on suddenly or in many repeated episodes over several months was the commonest clinical manifestation. Seizures, headaches, aphasia, blindness in one eye, and homonymous hemianopsia occurred with lesser frequency.

The mechanism of internal carotid artery thrombosis is obscure. The important factor may be a forward embolus arising from atheromatous plaques at the bifurcation, but this does not hold for all cases.

The diagnosis is best made by angiography. The indications for this procedure are the sudden onset of hemiplegia or hemiparesis, with clear spinal fluid under normal pressure, or repeated attacks of hemiplegia or hemiparesis, even though of short duration. The needle should be introduced low in the neck and a roentgen exposure including the neck should be made during the injection. A complete obstruction of the internal carotid artery may be demonstrated at the bifurcation of the common carotid or a short distance superiorly. The external carotid artery may remain patent for years, and may supply the means of vascularizing the brain through communications with the frontal and supraorbital branches of the ophthalmic artery. Optic atrophy and blindness are thus much less common with internal carotid artery thrombosis than in common carotid artery thrombosis with involvement of both the internal and external carotids.

The prognosis of internal carotid artery thrombosis is uncertain. A few of the younger patients appear to recover function following a period of disability. Treatment is generally unsatisfactory. It may include bilateral stellate block, excision of the cervical sympathetic on one or both sides, the use of anticoagulants, excision of the freshly formed clot, carotid artery ligation and excision of the thrombosed vessel, ligation of the carotid siphon intracranially, and finally rehabilitation. In all of the authors' cases stellate blocks were performed, but the results of this form of therapy were not encouraging. In 15 cases the carotid bifurcation was exposed and a portion of the thrombosed artery was excised. Of the total series of 30 patients, 8 appeared to have recovered satisfactorily, though the period of follow-up is short. The role of rehabilitation to mobilize such patients and to help them recover power in paralyzed limbs and regain speech is important.

Six roentgenograms; 1 diagram; 1 photomicrograph; 2 tables.

SEYMOUR A. KAUFMAN, M.D.
Boston, Mass.

THE CHEST

Water-Soluble Contrast Medium for Bronchography. M. Eugene Flipse, Gustav A. Hedberg, and Victor R. Krueger. *Arch. Otolaryng.* 57: 188-205, February 1953.

The authors' experience with "Xumbradil viscous B" (introduced by Morales and Heiwinkel—*Acta radiol.* 30: 257, 1948, and 32: 317, 1949. *Abst. in Radiology* 53: 303, 1949, and 55: 465, 1950—as Umbradil-Viskös B) in 79 bronchographies in 58 patients, including 38 with tuberculosis, is in accord with the nearly universally favorable experience reported with this and other iodopyracet-carboxymethylcellulose media. The technic was as follows: Premedication was minimal, consisting of 100 mg. of pentobarbital (Nembutal) sodium or secobarbital (Seconal) sodium by mouth one and a half hours before the procedure and subcutaneous injections of codeine and atropine three-quarters of an hour before. Topical anesthesia of the pharynx and larynx was obtained by spraying with minimal amounts of a 0.5 per cent solution of tetracaine hydrochloride. Meticulous intrabronchial anesthesia was secured with a freshly prepared 5 per cent solution of cocaine hydrochloride, first by drop-by-drop transglottic instillation and then by repeated instillation of small amounts through a soft rubber 14 or 16 F catheter placed in the trachea through the nose or the mouth. As the cocaine was instilled, the patient was positioned as if the contrast medium had been introduced and was encouraged to cough in each position to disseminate the anesthetic agent further. The dose of cocaine was limited to less than 8 c.c. of the 5 per cent solution. No epinephrine or other vasoconstrictor drug was added to any of the anesthetic agents. Consideration was given to the 0.5 per cent lidocaine solution, a local anesthetic agent, present in the "Xumbradil" in calculation of the total dose of anesthetic agent used.

For filling the bronchial tree with contrast medium, the authors used the three-position method described by Schmidt (*Ann. Otol., Rhin. & Laryng.* 56: 793, 1947. *Abst. in Radiology* 51: 125, 1948). The only modifications of the basic technic were shortening of the time the patient was left in each position and decrease of the angle of the head-down positions.

In the authors' 58 patients, 66 unilateral and 13 bilateral bronchograms were obtained. In 18 cases two or more "Xumbradil" bronchograms were made: in 11 cases to visualize the opposite side, in 6 cases because of previous failure to obtain a satisfactory bronchogram, and in 4 cases to verify apparent pathologic changes.

Sixty-two satisfactory bronchograms were obtained in 79 attempts. There were 17 unsatisfactory bronchograms in 14 cases, but satisfactory bronchograms were ultimately obtained in 7 of these, in 4 with "Xumbradil," in 2 with iodized oil, and in 1 with Methocel-Diodrast. In the 7 remaining failures, repeat bronchography with "Xumbradil" was unsuccessful in 1 case, and in this patient and in the remaining 6 patients further bronchography was not attempted. Coughing due to incomplete anesthesia, non-filling of portions of the upper lobes, and roentgenographic difficulties arising from the use of spot-film or Bucky-grid techniques were the chief and equally important causes of these failures. Improper position of the tracheal catheter, too much contrast medium, and poor cooperation of the patient were less frequent and largely preventable causes of failure.

Bronchograms obtained with "Xumbradil viscous B" showed much less density and contrast than those usually obtained with the iodized oil media and also less than those obtained with "Xumbradil" and other water-soluble media by bronchial catheterization and soft-film technics. Although the original Swedish workers maintained that satisfactory bronchograms with "Xumbradil" can be obtained only by the latter technic, the comparatively light roentgenograms obtained by the authors were of such quality that complete accuracy of diagnosis and localization was usually possible. In 15 cases in which it was possible to evaluate the accuracy of the roentgenographic study in surgical specimens, the preoperative bronchographic diagnosis was confirmed in all.

The few complications encountered were in no instance felt to be due to "Xumbradil" itself.

In none of the 38 tuberculous patients was there hematogenous or bronchial dissemination, and in none of the 4 in whom evidence of an increase in the tuberculous process was first observed at least three months after bronchography was that procedure felt to be even contributory.

Seven roentgenograms.

Delayed Films in Bronchography. A Preliminary Report. Herbert L. Abrams, Gerhard Hencky, and Henry S. Kaplan. *California Med.* 78: 104-106, February 1953.

The authors obtained bronchograms both immediately after injection of a contrast medium and after a delay of from thirty to sixty minutes "in many patients" [exact number not given]. They found the most satisfactory interval to be thirty minutes. The delayed films helped to exclude or confirm a diagnosis of bronchiectasis in one-third of the cases and were most often of value when the disease was in the middle lobe.

Delayed films should not be expected to compensate for careless technic. Every effort should be made to obtain good filling initially; when this is successful, further films are not needed. When, however, the initial study shows incomplete filling, delayed films may spare the patient a repetition of the oil injection.

Eight roentgenograms. JOHN J. CRAVEN, M.D.
Cleveland Clinic

Cinedensigraphic Study of the Pulmonary Arterial Circulation in Different Pathologic Affections of the Lung, Bronchi, and Mediastinum. R. Kourilsky and M. Marchal. *J. franç. méd. et chir. thorac.* 7: 113-125, 1953. (In French)

The cinedensigraphic method, a modification of electrokymography, was used to study changes in pulmonary circulation produced by various diseases. In alveolar inflammatory conditions of recent origin, whether tuberculous or non-tuberculous, there is very little or no modification of the circulation. In alveolar inflammations accompanied by cavitation, there is local diminution of circulation but no distant alteration. In chronic tuberculous infection, especially with fibrotic changes, there may be some decrease in circulation at a distance from the involved area, but in the affected lobe.

Bronchogenic diseases often show more circulatory change than pulmonary parenchymal diseases. In non-cancerous atelectasis, there is local diminution of the circulation. In atelectasis produced by carcinoma

both local and distant decreases occur. There is relatively little change in bronchiectasis, but in emphysema there is a general diminution of circulatory flow.

With enlarged tuberculous mediastinal nodes there may be discrete changes in the circulatory pattern. With Hodgkin's disease the change is more pronounced.

Circulation is diminished, but not abolished, by pleural thickening. Arterial circulation is diminished in pulmonary stasis caused by cardiac failure.

Five roentgenograms; 5 electrocardiograms; 2 drawings.

CHARLES NICE, M.D.
University of Minnesota

Involvement of Bone Marrow in Diffuse Pulmonary Disease. Austin S. Weisberger and Robert M. Dumm. *Arch. Int. Med.* 91: 212-223, February 1953.

A difficult diagnostic problem is frequently presented by the roentgen demonstration of discrete miliary opacities or other diffusely distributed lesions in the lungs. In an attempt to aid in the interpretation of such findings, the authors turned to a study of the bone marrow. Sternal aspirations were performed in 24 consecutive patients with diffuse pulmonary lesions and in 25 patients known to have far-advanced tuberculosis. Nine of the former group showed pathologic involvement of the marrow. The 9 cases included 3 of miliary tuberculosis, 2 of sarcoidosis, 2 of histoplasmosis, and 1 of amyloidosis; 1 case remained undiagnosed. With a single exception the marrow involvement was in the form of a granuloma. In 5 cases (3 of miliary tuberculosis, 2 of sarcoidosis) the diagnosis could be made on the basis of the marrow findings. In the remaining 15 patients with diffuse pulmonary lesions, the marrow was normal histologically. Several of these were known to have disease limited to the lungs, including 4 with pulmonary fibrosis, and some of the others are believed not to have had disseminated disease.

None of the patients with far-advanced tuberculosis were found to have lesions in the bone marrow, from which it is concluded that the roentgenographic appearance of miliary opacities is of more importance in indicating bone marrow involvement than the presence of extensive lung disease.

It is further concluded that examination of the marrow may be of diagnostic value in the presence of miliary opacities or diffusely distributed pulmonary lesions when disseminated granulomatous disease is suspected.

Seven roentgenograms; 9 photomicrographs; 2 tables.

Deformities of the Thorax of Congenital or Developmental Origin. Charles W. Lester. *J. Pediat.* 42: 195-204, February 1953.

Congenital and developmental deformities of the thorax are divided into two groups: (1) those due to absence or malformation of bony structures; (2) those caused by abnormal growth and the abnormal pull of the attached muscles.

In the first group are those deformities associated with absence of the ribs, incomplete ribs, fused ribs, forked ribs, and supernumerary ribs. The latter two types are not important and are usually discovered only by chance. When ribs are absent or incomplete, however, the associated muscles are also absent or malformed, causing rather definite deformity of the chest wall. Treatment varies with the location of the defect.

Fused ribs are important only when the fusion is posterior, in which event severe crippling deformities may result, requiring surgical correction.

In the second group are the protrusion deformities and the funnel chest. The protrusion may be in any part of the sternum, to either side of it, or below in the costal arch. The etiology of these protrusions is obscure, but they are presumed to be due to restraint of growth by the diaphragm or other muscles. Such restraint causes the growing ribs to buckle and produce the protrusion. These deformities are rarely noticed before the age of five. They may be responsible for prolonged respiratory infections, failure to gain weight normally, easy fatigability, and dyspnea and tachycardia. Surgical correction will rectify the condition in many cases.

The funnel chest is due to a short central tendon of the diaphragm which draws the xiphoid backward during inspiration. This deformity is noted at birth and becomes worse as the child grows older. There are often respiratory difficulties, poor posture, and poor development. Operative correction should be undertaken before fourteen months of age, when the procedure is relatively simple. Later, more extensive surgery is required.

All of the deformities of the thorax discussed can be easily distinguished on the roentgenogram and thereby properly classified and treated.

Six roentgenograms; 10 photographs.

PAUL W. ROMAN, M.D.
Baltimore, Md.

Agenesis of the Lung. Report of a Case, with a Review of All Previously Reported Cases. A. Oyama, B. M. Gasul, and P. H. Holinger. *Am. J. Dis. Child.* 85: 182-201, February 1953.

Agnetic malformations of the lung have been divided into three classes: Class 1 consists of cases in which no trace of a bronchus or lung is found; in Class 2, there is no lung tissue but some trace of a bronchus; in Class 3, the main bronchus is incompletely developed and there is hypoplasia of one or both lungs. The authors present a case of true agenesis with no trace of the lung, bronchus, or vascular supply on the right side. In a review of the literature they found 73 cases of congenital aplasia of one lung (Classes 1 and 2), in 25 of which the diagnosis was made during life. They also found 38 cases of hypoplasia of one or both lungs (Class 3), 13 of which were diagnosed during life. In addition, there were 4 cases of newborn infants with congenital absence of both lungs and 21 cases with either agenesis or congenitally hypoplastic lung in which the description was incomplete or the condition not definitely established by special clinical methods or by postmortem examination.

Two roentgenograms; 1 electrocardiogram; 2 photographs; 1 photomicrograph; 4 tables.

Histoplasmosis, with Review of the Literature and Report of a Case, Proved By Culture, with Involvement of the Upper Lobe of Each Lung Simulating Active Bilateral Apical Pulmonary Tuberculosis. James Monroe and Joseph M. Kurung. *Ann. Int. Med.* 38: 206-223, February 1953.

Recently, it has been repeatedly shown that many individuals having calcified pulmonary lesions and negative tuberculin reactions are sensitive to histo-

plasmin. In cases coming to necropsy, the frequency of involvement of the lungs by *H. capsulatum* is second only to that of the lymph nodes, the liver, and the spleen.

The authors report at length a case of bilateral upper lobe pulmonary histoplasmosis in a 56-year-old white male. The presumptive pre-admission diagnosis was pulmonary tuberculosis. The clinical course had been consistent with this diagnosis, and the tuberculin test was positive. For six weeks before admission the chest roentgenograms had shown evidence of chronic bilateral upper lobe pulmonary disease of mixed bronchopneumonic and cavitary types. Doubt was cast on the diagnosis of tuberculosis, however, when numerous examinations of the sputum failed to reveal the presence of tubercle bacilli but showed large amounts of elastic tissue. The coccidioidin skin test was negative, while the histoplasmin test was positive. The diagnosis of pulmonary histoplasmosis was established when cultures at both room and incubator temperature (37° C.) consistently showed numerous colonies of *H. capsulatum* but no other fungi.

Various types of pulmonary lesions have been described in patients with histoplasmosis, such as interstitial pneumonia, discrete or confluent areas of lobular pneumonia, miliary and larger nodules, granulomata, caseation necrosis, abscesses or cavities, fibrosis, and calcifications. The lack of a characteristic pattern of abnormality demonstrable on the chest roentgenogram reflects the absence of a specific or uniform type of lesion. Among 65 cases with proved involvement of the lungs by histoplasmosis reported up to Jan. 1, 1950, chest roentgenographic findings resembling the apical reinfection type of tuberculosis, as in the case reported here, were demonstrated in only 4. In only 3 cases was evidence of pulmonary cavitation seen.

The diagnosis of histoplasmosis can be established only by the demonstration of the fungus by laboratory methods. The great variability in the presenting symptoms and signs of this illness causes it to simulate many other diseases and thereby makes its clinical diagnosis difficult or impossible. It may exist as a chronic illness for years, with an eventual exacerbation which may prove fatal. The course and prognosis are exceedingly varied. In these respects it is comparable to tuberculosis.

This is the first case of proved histoplasmosis to be reported in a life-long resident of New York who had never traveled outside of the state.

Six roentgenograms; 5 photomicrographs.

STEPHEN N. TAGER, M.D.
Evansville, Ind.

Pulmonary Infarction Mistaken for Bronchogenic Carcinoma. Rex B. Perkins and H. H. Bradshaw. *J.A.M.A.* 151: 545-548, Feb. 14, 1953.

Two cases are reported with findings in the chest roentgenogram thought to represent carcinoma but which proved to be due to pulmonary infarcts. In the first case there was an isolated asymptomatic "coin lesion" in the periphery of the right lower lung field. The second patient was admitted to the hospital with a history of right chest pain and hemoptysis. Roentgenograms of the chest revealed "segmental atelectasis and infiltration" of the right middle lobe and "a nodular density about 3 cm. in diameter near the inferior portion of the right hilus." At operation there was found to be collapse of the lateral segment of the right middle

lobe and an aneurysm-like dilatation of the pulmonary artery at the hilus, apparently encroaching upon the bronchus to the lateral segment of the middle lobe. No other hilar lesion was found. The resected lateral segment of the middle lobe showed thrombosis of the pulmonary vessels with organization and pulmonary infarction. The hilar nodule seen on the roentgenogram represented a localized dilatation of the pulmonary artery, a phenomenon previously noted in association with infarct. Its cause is not clear, but it may be due to increased resistance to the blood flow, owing to the embolus. From a roentgenographic standpoint, infarction may mimic almost any other lung disease and should be considered in the differential diagnosis of suspicious pulmonary lesions prior to exploration.

Four roentgenograms.

SEYMOUR A. KAUFMAN, M.D.
Boston, Mass.

Pulmonary Complications of Cardiospasm. Howard A. Andersen, Colin B. Holman, and Arthur M. Olsen. *J.A.M.A.* 151: 608-612, Feb. 21, 1953.

From 1935 to 1946 inclusive, 601 patients with cardiospasm were observed and treated at the Mayo Clinic. Because more than 10 per cent of these patients had significant respiratory disease, it was considered that the pulmonary complications were deserving of special attention.

Aspiration pneumonia was the commonest finding in the series, including both focal and diffuse processes. It was present in 46 cases. The most frequent location, as evidenced by roentgenologic examination of the thorax, was the midportion of the right lung. When pneumonia was extensive and bilateral, the roentgenologic appearance occasionally simulated miliary tuberculosis, silicosis, or metastatic carcinoma. Acid-fast bacilli sometimes were found but in at least one case, these organisms proved to be saprophytic.

Pulmonary fibrosis of sufficient degree to be considered an end result of aspiration pneumonia was present in 3 cases. Typical bronchiectasis occurred in 5 cases, and a lung abscess in 1 instance. Four patients had acute episodes that simulated bronchial asthma and two of these were greatly improved after treatment for cardiospasm. Two patients had rather extensive emphysema.

The authors feel that in patients with pulmonary infiltrations simulating aspiration pneumonia, it is well to consider the possibility of esophageal obstruction as the etiologic factor. Inasmuch as effective methods of treating cardiospasm are available, the relatively high incidence of pulmonary complications provides an additional reason for prompt institution of treatment after cardiospasm has been recognized.

Seven roentgenograms; 1 diagrammatic drawing.

L. R. JAMES, M.D.
Boston, Mass.

Pulmonary Edema in Acute Opium Intoxication. Philip Troen. *New England J. Med.* 248: 364-366, Feb. 26, 1953.

Acute opium intoxication is not commonly seen in American medical practice. A probable increase in incidence, however, may be expected in view of the evidence of widespread drug addiction and the possible exposure of the uninitiate to accidental and intentional overdosage of opium derivatives. The diagnosis of

acute opium intoxication should be suggested by the classic triad of coma, greatly depressed respirations, and pin-point pupils. In the case reported here, from an Army Hospital in Japan, pulmonary edema was also a part of the clinical picture.

Unless pulmonary edema is expected or is detected on routine x-ray studies of the chest, its presence may not be appreciated. The edema is unlike that associated with cardiovascular disease. It is evidently chiefly interstitial, without a marked alveolar component; râles and other direct signs, except cyanosis, are rare.

The mechanisms of pulmonary edema in acute opium intoxication are not clear. The marked depression of the respiratory center and the possibility of direct pulmonary irritation after intravenous administration are of possible significance.

The importance of the pulmonary edema of acute opium intoxication is indicated by its response to therapy. The primary goal is correction of anoxia, and measures to stimulate respiration and preserve adequate pulmonary ventilatory function are important. These measures include artificial respiration as well as Coramine and caffeine and perhaps some of the newer agents. Intensive and continuous oxygen therapy is necessary. Gastric lavage, preservation of a pharyngeal airway, maintenance of body temperature, prevention of aspiration, change in position, and prophylactic chemotherapy are valuable adjuncts.

Four roentgenograms. L. R. JAMES, M.D.
Boston, Mass.

Plasmacytoma of the Lung. Lucius D. Hill, III, and M. Lawrence White, Jr. *J. Thoracic Surg.* 25: 187-193, February 1953.

A case is reported of a 3-year-old white girl with a plasmacytoma of the lung. A left total pneumonectomy was done, with no evidence of recurrence or metastasis after eight years.

Roentgenograms of the chest prior to operation revealed a large rounded opacity which nearly filled the left hemithorax, displacing the heart and mediastinum to the right. Changes characteristic of pulmonary osteoarthropathy were present in all the long bones. The patient was given a course of x-ray therapy, but examination following completion of treatment showed an apparent increase in size of the mass. A thoracotomy was then done, and a large dense mass was found occupying all of the lower lobe and extending across the interlobar fissure into the upper lobe. Nineteen months after pneumonectomy the osteoarthropathy had completely disappeared and the left thorax was filled with lung from the right side.

A review of the literature reveals only 4 cases of extramedullary plasmacytoma believed to have originated in the lung, and in 1 of these the evidence for a pulmonary origin is not conclusive.

Considerable confusion exists concerning the origin and behavior of this tumor. Plasma cells, according to recent evidence, are probably derived from both fixed and emigrated lymphocytes, and plasmacytoma may bear some relationship to tumors of lymphatic tissue. It should be considered malignant, and surgical removal is the treatment of choice, provided there has been no metastasis or invasion of vital structures.

Two roentgenograms; 1 photomicrograph.

SEYMOUR A. KAUFMAN, M.D.
Boston, Mass.

Bronchogenic Cysts. A Manifestation of Congenital Polycystic Disease of the Lungs. Elwyn L. Heller, James H. Householder, and Albert M. Benshoff. *Am. J. Clin. Path.* 23: 121-128, February 1953.

A bronchogenic cyst may occur at any age, the majority being found in young or middle-aged adults, without predilection for either sex. Many cases are asymptomatic, but in a significant percentage symptoms have been present, as pain, cough, hemoptysis, or dyspnea.

The radiologic findings serve as the most valuable preoperative diagnostic feature. When there is no patent connection with the bronchial system, the cysts are distended with a thick mucinous fluid which is radiologically opaque and the lesion on the x-ray film appears dense, sharply circumscribed, and generally round or oval. In most cases in which communication with the bronchial system has been established, the sharply outlined cyst is air-containing, its wall is generally free of significant reaction and, on occasions, a fluid level may be evident.

The cyst in most cases is located centrally within or adjacent to the mediastinum. Pathologically it consists of a thin-walled round or ovoid cystic mass. It may be pedunculated or intraparenchymal. The inner lining is smooth, thin, and glistening.

Microscopically the most characteristic feature is the lining membrane, which consists of a single layer of columnar epithelium of respiratory type in which cilia can generally be demonstrated. Within the wall, tissues of the type forming the normal bronchus may be observed.

The authors have studied the pathologic specimens of 7 cases of "solitary" cyst of the lung. In 2 cases, in addition to the large bronchogenic cyst, cystic disease of a minor degree was present. The microscopic study of the associated small cystic lesions revealed features identical with those of the large cyst. From this it was concluded that the bronchogenic cyst is an incompletely developed manifestation of the well known congenital polycystic disease of the lung.

One photograph; 4 photomicrographs; 1 table.

HOWARD L. STEINBACH, M.D.
University of California

Multiple Tuberous Ossifications in the Lungs. J. Holý, F. Jindrák, and K. T. Veselý. *Acta radiol. et cancerol. bohemoslov.* 7: 29-38, Feb. 28, 1953. (In Czechoslovakian, with English summary)

Four cases of disseminated osseous nodules in the lungs are described. Two of these were confirmed post-mortem; 1 case did not come to autopsy and in the other the lungs were not examined with this condition in mind. The x-ray picture was typical in all cases. Mitral stenosis and pulmonary congestion were present in every instance. The authors believe that these disseminated osseous deposits arise on the basis of a rheumatic pneumonitis with simultaneous congestion.

Eight illustrations, including 4 roentgenograms.

Mediastinal Lymphosarcoma in an Infant. Twelve-Year Survival Following Radiation Therapy. Melvin H. Stich, Joshua Rubinstein, Asa B. Friedman, and Maurice Morrison. *J. Pediat.* 42: 235-238, February 1953.

The survival of an infant with mediastinal lymphosarcoma twelve years after radiation therapy is worthy

of note. When the child was first seen, at the age of seven months, cough and fever were the predominant symptoms. A chest roentgenogram revealed a large mediastinal mass, and biopsy was recommended. The parents, however, failed to return with the infant until seven months later. A repeat roentgenogram at that time showed little apparent change in the mass. A needle biopsy was done and reported as showing large-cell lymphosarcoma. Radiation therapy (factors not given) was delivered during the course of a month, a total dose of 1,360 r being given to the chest, half anteriorly and half posteriorly. Seven months later, the chest appeared normal on x-ray examination. The child has been followed continuously for twelve years and is clinically well.

Three roentgenograms; 2 photomicrographs.

PAUL W. ROMAN, M.D.
Baltimore, Md.

Chronic Massive Thrombosis of Pulmonary Arteries. A Report of Seven Cases with Clinical and Necropsy Studies. D. R. Keating, J. N. Burkey, H. K. Hellerstein, and H. Feil. *Am. J. Roentgenol.* 69: 208-220, February 1953.

This paper deals with the most unusual type of pulmonary artery obstruction, namely that characterized by slowly developing thrombosis of the pulmonary arterial tree with progressive right ventricular failure. Seven cases are reported.

Various cardiac and pulmonary vascular diseases may result in local thrombus formation in the pulmonary artery and its branches. These fall generally into two categories. In one, primary lung disease, such as infection or tumor, directly involves the pulmonary arterial tree and leads to pulmonary thrombosis with propagation of the clot. The other is characterized by diffuse vascular disease of the lungs, usually secondary to degenerative or chronic inflammatory disease or to mitral stenosis, but occasionally the result of a primary vascular inflammatory process. Here the following events occur: (a) pulmonary hypertension; (b) hypertrophy of the right ventricle; (c) right heart failure; (d) thrombosis of the pulmonary artery which aggravates the existing disease and results in sudden death.

Patients who have had pulmonary emboli, and those suspected of primary cor pulmonale from whatever cause, appear to be most likely to develop pulmonary thrombosis.

The symptoms of pulmonary artery thrombosis are often those of ordinary congestive failure. Since the formation of thrombi is usually unsuspected, the diagnosis is seldom made before death. The occurrence of thrombi is commoner in the older age groups, but cases have been reported in children, and, in the presence of antecedent emboli, chronic massive thrombosis may occur at any age.

The electrocardiogram shows a tendency to right axis deviation, and a change from left to right axis deviation may be observed over a period of months.

Of specific interest to the roentgenologist are the changes which result from ischemia of the lung peripheral to the intravascular occlusion, manifested by diminished vessel markings in the part of the lung supplied by the affected arterial branches. These peripheral vessels are contracted and relatively devoid of blood distal to the point of obstruction. They are small and reduced in visible number, producing the net

roentgenographic effect of segmental blackening of the lung fields. In the event of embolism or thrombosis involving a major branch, the affected vessels will often be enlarged at the point of obstruction and dilated proximally to it in a manner to provide a clue to the diagnosis.

The difficulty in accurate roentgenographic diagnosis of this relatively rare condition is the common association of cor pulmonale with enlarged pulmonary arteries and pulmonary emphysema, the latter simulating the much less common pulmonary ischemia. Enlarged lymph nodes may present a diagnostic problem. The tapering effect characteristic of the pulmonary arteries as their descending branches diminish in caliber inferiorly will in most cases serve to distinguish them from other structures. It is also necessary to differentiate an abnormal hilar mass with segmental emphysema (bronchogenic carcinoma) from an abnormal hilar mass with segmental ischemia (thrombosis).

When the syndrome of right heart failure exists without pulmonary congestion, indicating that obstruction is present in the lesser circulation, a diagnosis of chronic massive thrombosis of the pulmonary arteries is to be considered.

Thirteen roentgenograms; 4 electrocardiograms; 3 tables.

JOHN F. BERRY, JR., M.D.
Louisville General Hospital

Secondary Tumors of Heart and Pericardium. Review of the Subject and Report of One Hundred Thirty-Seven Cases. James F. DeLoach and James W. Haynes. *Arch. Int. Med.* 91: 224-249, February 1953.

In a series of 2,547 consecutive autopsies performed at the Walter Reed Army Hospital over an eleven-year period, 980 cases of malignant neoplastic disease were observed, and in 137 of these (13.9 per cent) there were metastatic lesions in the heart and pericardium. Carcinoma invaded the heart and pericardium more frequently than did any other malignant process, with a rate of 21 per cent of 105 cases. Lymphatic leukemia showed practically the same percentage but the case total was only 62. An antemortem diagnosis was made in 3 cases, 1 of which is presented in detail here. Four other cases with significant clinical, laboratory, or necropsy findings are also reported.

Among the features listed by the authors as suggestive of the diagnosis, in the absence of other more common causes, are radiologic evidence of an irregular or unusual heart border and relative immobility of the right border of the heart as demonstrated fluoroscopically.

In 2 of the series reported there was roentgen evidence of cardiac tamponade and in 17 cases cardiomegaly was shown roentgenographically.

Fourteen illustrations, including 3 roentgenograms; 4 tables.

Complete Transposition of the Great Vessels. Robert F. Rushmer, Dean K. Crystal, Robert A. Tidwell, R. F. Crose, and John A. Hendron. *J. Pediatr.* 42: 189-194, February 1953.

Complete transposition of the great vessels presents a clinical picture which can usually be recognized. When the diagnosis is made, surgical correction should be done if at all possible. Normally the septum which during embryologic development divides the aorta and pulmonary artery is a spiral which swings through 180°

and joins with the interventricular septum. This causes the left ventricle to fuse with the aorta and the right ventricle with the pulmonary artery. In complete transposition of the great vessels, this septum remains straight. As a result, the left ventricle empties into the pulmonary artery and the right ventricle into the aorta. Blood from the left ventricle flows through the lungs and is oxygenated, returning to the left side of the heart. Therefore, oxygenated blood can reach the systemic circulation only through shunts, such as septal defects and a patent ductus arteriosus. The clinical syndrome includes cyanosis beginning immediately after birth, increased blood flow and blood content in the pulmonary vessel, right ventricular preponderance, progressive cardiac enlargement, retarded growth and development, and angiocardigraphic evidence of continuity between the right ventricle and the aorta.

Two cases are described. In the first case angiocardigraphy was not done but all the other above mentioned features were present. A Blalock operation was performed, but the child died suddenly on the third postoperative day.

In the second case, angiocardigraphy was done through a polyvinyl catheter in the left jugular vein. The opaque material was followed by cinefluorographic recording on 35 mm. film exposed at 15 frames per second. There was evidence of a small interatrial septal defect, but the bulk of the material passed into the right ventricle and then to the aorta. The left side of the heart was not opacified at any time. This patient suddenly died thirty-six hours after the examination, and the diagnosis was confirmed at autopsy.

Three roentgenograms and 1 cinefluorographic series; 2 drawings; 1 photograph.

PAUL W. ROMAN, M.D.
Baltimore, Md.

Patent Ductus Arteriosus and Congenital Mitral Stenosis. A. de Carvalho Azevedo, M. Barreto Neto, Aparecida Garcia, and A. Alves de Carvalho. *Am. Heart J.* 45: 295-304, February 1953.

The association of patent ductus arteriosus and mitral stenosis is extremely rare. A case is presented in an 18-month-old girl brought for treatment on account of dyspnea and fatigue. There was a distinctly heard diastolic murmur over the precordium, maximum at the apex, with the characteristics of a rumble.

A roentgenogram of the chest showed an enlarged heart with a small vascular pedicle. The shadow of the left bronchus was displaced upward, and the left auricle was increased in size. There was congestion of the lungs. An angiocardigram revealed filling of the descending aorta simultaneously with the opacification of the pulmonary artery. At the time the opaque medium was in the left side of the heart, the ascending aorta could be visualized, but not its descending portion. It was concluded that the premature opacification of the aorta was due to a venous-arterial shunt through a patent ductus arteriosus, and the non-visualization of the descending aorta on the levoangiocardigram was attributed to the dilution of the contrast medium in the aorta by the blood flow coming from the pulmonary artery. The persistence of opacification for two seconds, in the levoangiocardigram, suggested the presence of a mitral stenosis.

The child was operated upon and the ductus was ligated. Death occurred two hours after surgery. Au-

topsy revealed the presence of patent ductus arteriosus and mitral stenosis.

Six roentgenograms; 4 drawings; 1 photocardio-gram; 1 electrocardiogram; 3 photographs; 2 photomicrographs.

HOWARD L. STEINBACH, M.D.
University of California

THE BREAST

Some Contributions of Radiology to the Pathology of the Female Breast. J. Gershon-Cohen and H. Ingleby. *Brit. J. Radiol.* 26: 87-92, February 1953.

Radiography of the female breast has not been generally accepted as of diagnostic value for several reasons, notably faulty x-ray technic, inexperience of the radiologist, poor standardization of nomenclature, and insufficient correlation of x-ray and histological technics. The authors have worked out certain criteria as a result of careful x-ray study of 400 breasts, comparing them with serial whole breast sections.

Lateral and tangential breast films and spot films of diseased areas are made at about 30 kv. with the smallest available focal spot (1.2 mm.) and non-screen film. The target-film distance varies with the distance of the lesion from the film, from 25 to 75 cm. If the lesion can be brought close to the film, the shortest possible film-target distance is used. [The technic is described in *Radiology* 60: 68, 1953.]

Comparing the films with serial sections, a classification mutually satisfactory to the pathologist and radiologist was worked out:

1. Mazoplasia
 - Group I
 - Group II
2. Adenosis (unencapsulated lobular hyperplasia)
3. Fibroadenoma
4. Secretory disease
5. Papilloma
6. Mastopathy (Schimmelbusch's disease)
7. Carcinoma

Mazoplasia I, showing increase in the intraductal fibrous tissue, is the mazoplasia of Cheate and Cutler. In Mazoplasia II, simple cysts are present. Secretory disease is indicated by simple blurring. Carcinoma is indicated by an abnormal mass plus thickening and distortion of the trabeculae. Benign disease simply displaces the trabeculae. Ductal carcinomas show minute punctate spots of calcification following the lines of the ducts. Other carcinomas may show occasional spots of calcification.

Four roentgenograms; 5 photomicrographs.

SYDNEY J. HAWLEY, M.D.
Seattle, Wash.

THE DIGESTIVE SYSTEM

Barium Studies of the Comparative Action of Banthine, Tincture of Belladonna and Placebos on the Motility of the Gastrointestinal Tract in Man. William P. Chapman, Stanley M. Wyman, Lidio O. Mora, Margaret A. Gillis, and Chester M. Jones. *Gastroenterology* 23: 234-243, February 1953.

The authors have studied the comparative action of Banthine, tincture of belladonna and placebos on the motility of the gastrointestinal tract in man by a modification of a barium method previously described by others (Lepore *et al.*: *Gastroenterology* 17: 551,

1951. *Abst. in Radiology* 58: 455, 1952). They sought to ascertain two facts: the time required for gastric evacuation and the distance traveled by the head of the barium meal along the intestine after injection of the various drugs. Eighty-seven studies were made in 13 subjects, and each subject was tested with all three agents, usually on at least two occasions.

A drug or placebo was given at 8:00 A.M. and the barium at 9:00 A.M. At 9:15, 10:00 and 12:00 roentgenograms were obtained in the supine position.

Banthine, given in a dose of 100 mg. orally, caused a more striking decrease in the movement of barium along the intestine and in the delay of gastric evacuation than was noted with either the placebo or tincture of belladonna. There were no differences between the belladonna and placebo results for gastric evacuation.

Side-reactions were not a striking feature in any of the studies with the exception of dryness of the mouth and scratchy or sore throat. These reactions were somewhat more prominent with Banthine than with the tincture of belladonna.

These preliminary results indicate that the barium technic is a useful method for comparing the action of drugs on the propulsive activity of the stomach and intestine in man.

Two series of roentgenograms; 5 charts; 1 table.

L. R. JAMES, M.D.
Boston, Mass.

Roentgen Reexamination of the Gastrointestinal Tract. George H. Stein, Irving I. Lomhoff, Ethel Stuteville, and Carlos V. Garcia. *Permanente Found. M. Bull.* 10: 320-326, February 1953.

Re-examination of the esophagus, stomach, small and large bowel, as well as of the gallbladder, may be necessary for accurate evaluation of previous findings or to search further for a lesion which may have been missed on the initial examination.

Re-examination by a double-contrast technic is particularly useful in polypoid lesions of the stomach and large bowel. It also helps to establish the constancy of these small filling defects. Frequently, re-examination may be the chief means of differentiation of benign and malignant ulcers in the stomach, and repeated studies may distinguish between diverticulitis and carcinoma of the large bowel.

The non-visualized gallbladder is a good example of the value of repeat studies. The polyp or adenoma of the gallbladder often calls for a check upon the constancy and position of the abnormal density prior to surgery. Cholesterol stones may not be identified at first and may require further study by special technics.

Re-examination may be indicated, also, when there is a discrepancy between clinical and radiologic findings, when new clinical or laboratory information has become available, for determination of healing of benign lesions, and prior to surgery if some time has elapsed since the last examination.

Six illustrative cases are reported.

Twenty-eight roentgenograms.

M. HARLAN JOHNSTON, M.D.
Jacksonville, Fla.

Roentgenologic Considerations of Gastro-Intestinal Lesions Causing Hematemesis. Robert D. Moreton. *South. M. J.* 46: 127-135, February 1953.

The author discusses the roentgenographic characteristics of the more common causes of bleeding from

the upper gastrointestinal tract. Twelve illustrations show examples of carcinoma of the esophagus, hiatus hernia with ulceration, gastric and duodenal ulcers, gastrojejunal ulcers, and gastric and duodenal neoplasms.

Regardless of the care in examination, including gastroscopy and surgical exploration, there are some 15 to 17 per cent of cases in which no pathologic condition is found. The importance of early examination is emphasized. The cause of bleeding is demonstrated in a higher percentage of cases if the examination is done during the time of bleeding. JOHN M. KOHL, M.D.
Jefferson Medical College

Photofluorography for the Detection of Unsuspected Gastric Neoplasms. Russell Wigh and Paul C. Swenson. *Am. J. Roentgenol.* 69: 242-267, February 1953.

This is a review of the experiences of the authors with the 70-mm. photofluorograph for the screening of unsuspected gastric lesions in 5,096 patients. In this group of relatively asymptomatic patients of forty years or older, 11 "concealed" gastric neoplasms were found. Three proved to be carcinoma at operation; 1 probable carcinoma was not considered operable because of a co-existing cardiac abnormality. Five patients had proved benign adenomas of the stomach, and in 2 additional cases a diagnosis of adenoma was made but surgery was refused. The incidence is thus 2.1 concealed neoplasms per thousand examinations or 0.6 carcinoma per thousand examinations.

This article is quite lengthy, with a considerable amount of space devoted to financial considerations, as well as a discussion of the incidence of carcinomas and other stomach lesions as reported by others. An extensive review of the literature is given.

The authors feel that their photofluorographic method is simple, safe, and accurate, and that it is suitable for large population groups.

Twenty-four roentgenograms; 11 tables.

EVERETT L. PIRKEY, M.D.
University of Louisville

Radiologic Appearances in a Case of Lipoma of the Stomach. F. Hueber. *Ann. radiol. diag.* 25: 207-213, 1952-53. (In Italian)

A 54-year-old woman gave a three-year history of non-specific epigastric pain and post-prandial heaviness. Radiologic study of the stomach showed a defect in the greater curvature in the region of the antrum, interpreted as due either to extrinsic compression or to a mass within the wall of the stomach but not disturbing its normal pliability. Surgical exploration disclosed a submucosal lipoma in this area, about the size of an egg.

Review of the films showed an area of radiolucence less intense than that produced by intestinal gas but more than that of the surrounding abdominal soft parts. This shadow corresponded to the resected tumor in respect to size, shape, and position. The author believes that a specific diagnosis of lipoma could have been made on the rational grounds of the characteristic radiographic density of fat. [This is in line with the roentgenologic diagnosis of other lipid-containing accumulations, such as lipoma in the limbs and brain, dermoid cysts in the pelvis, etc.—C. V. C.]

Four roentgenograms.

CHRISTIAN V. CIMMINO, M.D.
Fredericksburg, Va.

Failure of Surgery to Relieve Symptoms in Prolapse of the Gastric Mucosa Through the Pylorus. Emanuel M. Rappaport, Abe Alper, and Eugene O. Rappaport. *Ann. Int. Med.* 38: 224-233, February 1953.

It is the authors' opinion, as previously stated (*J.A.M.A.* 150: 183, 1952), that prolapse of the gastric mucosa through the pylorus is a relatively common radiologic finding, being observed in the absence of digestive complaints and in conjunction with all the common diseases of the gastrointestinal tract. When symptoms occur, they are believed to be attributable, as a rule, to the primary disorder, the prolapse *per se* playing an insignificant role. The report of Kaplan and Shepard of favorable results in a series of cases treated surgically (*J.A.M.A.* 147: 554, 1951. *Abst. in Radiology* 59: 456, 1952) is criticized as being based on an inadequate follow-up period.

Four cases are reported here in which a recurrence of symptoms followed elimination of the herniated mucosa either by gastric resection or local excision. Since 3 patients experienced relief for periods ranging from four to seven months after surgery, an assessment of results on the basis of a three-month follow-up would have been most favorable. In each instance, however, there had been even longer periods of spontaneous remission prior to operation. The poor surgical results can be attributed directly to the fact that the symptoms were unrelated to the extrusion of gastric mucosa into the duodenum.

In accord with their theory, the authors conclude that all other causes for gastric complaints, both organic and functional, must be considered before subjecting the patient to surgery for mucosal prolapse. In the event of repeated upper gastrointestinal hemorrhage requiring surgical intervention, where no abnormality other than prolapsing gastric mucosa is found radiologically, and the cause of previous hemorrhage cannot be determined even at operation, a high subtotal gastric resection should be done rather than mere excision of the redundant antral mucosa. The more drastic procedure will at least safeguard against further hemorrhage from a peptic ulcer commonly associated with prolapsing gastric mucosa and not always detected at operation.

Three roentgenograms; 1 photograph.

STEPHEN N. TAGER, M.D.
Evansville, Ind.

Mechanism of Pain in Peptic Ulcer. Julian M. Ruffin, George J. Baylin, Clarence W. Legerton, Jr., and E. Clinton Texter, Jr. *Gastroenterology* 23: 252-264, February 1953.

The mechanism of the production of pain in peptic ulcer has been a source of controversy for years. The three main schools of thought are as follows: (1) that the pain is due to chemical irritation of pain fibers in the ulcer by hydrochloric acid; (2) that the pain is due to muscular activity of the stomach and duodenum; (3) that the pain is the result of reflex disturbance of the motor mechanism of the stomach and duodenal cap, initiated by stimulation of afferent nerves in the base of the ulcer by acid chyme. Inasmuch as both the hydrochloric acid and motility are variables, it was felt that one must be rendered constant in order to determine the influence of the other on the production of ulcer pain. In this study, the acid values were rendered relatively constant at a high level, and the relationship between motility and the ulcer pain was studied.

Eighty-eight patients having active ulcers with typical pain were given 200 c.c. of 0.1 N HCl (pH 1) in 100 "acid tests." In 66 cases, 2 ounces of barium sulfate were added to the hydrochloric acid. The suspension was administered orally or by Levin tube, and the patients were observed fluoroscopically at frequent intervals for a period of thirty minutes. The relationship between motility, "acid barium" at the ulcer site, and the presence or absence of ulcer pain was studied. The effects of certain drugs capable of altering autonomic activity were noted, and clinical observations of the patients were continued for several days.

The authors' results lead them to believe that hydrochloric acid *per se* is not necessarily the cause of ulcer pain, since, despite high acid values, only 37 tests were positive for pain. In these cases the pain was invariably associated with abnormal motility, appearing when motor function became abnormal and ceasing when it returned to normal. This abnormality consisted in inco-ordinated activity of the antral evacuation mechanism, with or without localized spasm. Of 39 patients with negative tests, examined fluoroscopically, none showed such abnormalities.

Since prompt relief of ulcer pain by ganglionic blocking agents has been reported, Bantline was given to 26 patients, and in 25 of these produced prompt relief. This coincided exactly with cessation of abnormal motility and relaxation of the stomach.

From these observations a concept is advanced that abnormal motility is the fundamental mechanism through which ulcer pain is produced. For the production and perception of ulcer pain there must be (1) a stimulus, hydrochloric acid or others less well understood; (2) an intact motor nerve supply to the stomach and duodenum; (3) altered gastroduodenal motility; (4) an intact sensory pathway to the cerebral cortex.

Three roentgenograms; 4 tables.

L. R. JAMES, M.D.
Boston, Mass.

The Incidence of the Coexistence of Gastric and Duodenal Ulceration. Maurice Feldman. *Gastroenterology* 23: 304-308, February 1953.

The author has brought together and tabulated cases of coincident gastric and duodenal ulcer collected from various sources as reported in the literature. The sources include autopsy, surgical, radiological, and clinical studies. A marked variation was found in the incidence of cases of associated gastric and duodenal ulcers in the various series reviewed and also, more specifically, from category to category. It was lowest (0.32 per cent) in general autopsy studies and roentgen studies (0.15 per cent) and highest among clinical series of benign gastric (17.4 per cent) and malignant ulcer cases (24.6 per cent).

It becomes apparent that data obtained from clinical sources would yield the most accurate information concerning the incidence, providing follow-up studies were made during the lifetime of the patient. However, since this type of study is difficult and rarely made, one must rely on autopsy records of peptic ulcer cases in which a careful inspection is made not only for the presence of ulceration but also for scar formation of healed ulcers. A conservative estimate of the clinical incidence of the association of gastric and duodenal ulcers is about 10 per cent. This incidence closely parallels the author's autopsy finding of 11 per cent among cases of peptic ulceration.

An interesting discussion is included on the association of gastric and duodenal ulcers and also the time of development and position of each.

One table.

L. R. JAMES, M.D.
Boston, Mass.

Differential Diagnosis of Small Bowel Ileus. E. Freeb. *Fortschr. a. d. Geb. d. Röntgenstrahlen* 78: 141-152, February 1953. (In German)

Fluoroscopy of the abdomen in erect position without a contrast medium is important in the differential diagnosis of small bowel obstruction. In adults, gas in the small bowel is nearly always pathological. In the rare exceptions to this rule, the gas forms fine blebs and passes rapidly through the bowel. In the case of clinical symptoms of ileus, the presence of gas is diagnostic.

The concomitant fluid level is wider than the gas shadow above it in the small bowel. In the large bowel, on the contrary, the gas shadow is wider. If the ileus is mechanical, peristalsis and contractions alternately increase and decrease the fluid level. If the ileus is paralytic, the bowel is completely motionless and fluid levels are uniformly distributed in both the small and large intestine.

A fluid level does not always mean ileus. Enemas may produce fluid levels, as may saline laxatives, constipating agents, enteritis, sprue, allergic reactions. Occlusion of the inferior duodenal loop may cause gas accumulation and dilatation in the duodenal loops and in the stomach.

Initially an air collection may be observed in the small bowel, without fluid level. In mechanical small bowel ileus, the large bowel may be entirely empty.

The author observed over a period of nine months 10 cases showing different radiological appearances of the gas shadows in small bowel ileus. The plain film does not always localize the site of the occlusion, though usually it is adequate for surgical indications. Absence of fluid levels does not contradict a clinical diagnosis of ileus. Preliminary enemata may prevent the diagnostic usefulness of the roentgen examination.

Nine roentgenograms. LEWIS L. HAAS, M.D.
Chicago, Ill.

Acute Appendiceal Abscess Simulating Cecal Neoplasm. Frank Ciampa, G. Stanley Miles, and Lawrence Andreson. *Arch. Surg.* 66: 171-173, February 1953.

A 42-year-old male was admitted to the hospital with a four-day history of constipation of rather sudden onset, accompanied by low abdominal colicky pain and upper abdominal distention. There was no previous history of gastrointestinal symptoms, weight loss, or fatigue. Physical examination was essentially negative. The x-ray examination revealed a constriction at the mid-ascending colon, suggesting either cancer or an inflammatory lesion. At operation, a large granulomatous mass was found involving the appendix and mid-ascending colon. The appendix had apparently ruptured, and its tip had become incorporated in the wall of the colon. The patient made an uneventful recovery.

The similarity on the x-ray examination between appendiceal abscess and cancer with obstruction is pointed out, and the importance of differentiating between the two is stressed. The surgeon should be pre-

pared to carry out an ileocolic resection if it should be necessary.

One roentgenogram.

SEYMOUR A. KAUFMAN, M.D.
Boston, Mass.

Meckel's Diverticulum. A New Roentgen Diagnostic Sign and Case Report. Henry H. Lerner, Samuel S. Levinson, and A. Eugene Kateman. *Am. J. Roentgenol.* 69: 268-271, February 1953.

A new roentgen sign is described which may aid in the diagnosis of Meckel's diverticulum, namely, the visualization of the air-outlined diverticulum on the survey roentgenogram of the abdomen. In one case the authors visualized a Meckel's diverticulum completely, including its neck leading to a segment of small intestine. In 2 other cases it was possible to make a tentative diagnosis.

A brief history of Meckel's diverticulum is given, followed by Edwards' classification of diverticula (*Brit. J. Radiol.* 22: 437, 1949. *Abst. in Radiology* 55: 146, 1950).

While Meckel's diverticula have been diagnosed roentgenologically by several workers, no case has been reported in which the air-filled diverticulum was revealed on a survey film. In a few cases, the demonstration has been made by barium enema. In others, the presence of an abnormal appearing loop of small intestine or a residual pocket of barium in the diverticulum has aroused suspicion leading to the diagnosis. The new sign poses some differential problems. Other possibilities to be kept in mind, though unusual, are pneumatosis intestinalis, abscess with gas-forming organisms, postoperative accumulations of air (*i.e.*, kidney bed, etc.), and lipoma of the mesentery. The clinical picture should be of aid in making the differentiation. Filling the diverticulum with barium during the gastrointestinal series confirms the diagnosis.

In the case reported here, the survey roentgenogram showed a large, ovoid gas-filled pouch in the left upper quadrant, tapering to a funnel shape at its inferior pole. On barium enema examination, the colon filled well, with spilling out of the barium into the terminal ileum and into the diverticulum.

Two roentgenograms; 1 photograph.

CLAUDE D. BAKER, M.D.
University of Louisville

Roentgen Examination of the Deep Rectogenital Pouch. Lennart Walldén. *Acta radiol.* 39: 105-116, February 1953.

The rectogenital pouch, the most inferior part of the peritoneal cavity, forms a fissure-like space between the rectum and the intrapelvic genital organs. The inferior tip of the pouch ordinarily lies at the level of the posterior vaginal fornix or at the upper border of the prostate. A deep rectogenital pouch may reach down to the pelvic floor or may protrude through it in hernia-like bulges. It may project into the vagina or rectum, in which case the bulge is covered by the posterior vaginal wall or the anterior rectal wall. If the protrusion presents through the anus, there is a true rectal prolapse.

The author has presented a previous report (*Acta chir. scandinav.*, Suppl. 165, 1952) concerning the pathogenesis, clinical signs, and roentgenology of the deep rectogenital pouch, the main theme of which was

association of the anatomic anomaly with a defecation disorder in which there was the sensation of blocking of the rectum while straining at stool. Palpation in these cases shows the anterior rectal wall bulging down and obstructing the ampulla or, in extreme cases, the anorectal ring. The deep rectogenital pouch may be an isolated anomaly or associated with uterine prolapse or ptosis of other pelvic organs.

A parallel is drawn between the congenital deep rectogenital pouch and a patent processus vaginalis peritonei. The former may remain latent until, filled with intestines, it gives rise to symptoms or is disclosed by examination.

The author has studied 12 cases in men and 29 in women—the defecation block series—with a control series of 104 healthy subjects, aged four to sixty, for comparison. The difference between the two groups with regard to the mean position of the intestines and colon in the rectogenital pouch and the relation to the pelvis was considered in the earlier publication. The object of the present paper is to give an account of the examination technic and to illustrate a few cases of deep rectogenital pouch regardless of symptoms.

A barium enema is administered under fluoroscopic control and is stopped when it reaches the descending colon. An upright film is obtained in the lateral projection, and two post-evacuation films are made, one with maximal straining. A barium meal is then given, divided into two portions, two hours apart, since this accelerates passage through the small bowel. When fluoroscopy reveals a complete and uniform distribution, an anteroposterior and two lateral films, one with straining, are obtained. These views of the pelvis give a picture of the relation of the contrast-filled bowel to the bony pelvis.

There is a normal variation in the level reached by the bowel but the inferior margin is usually at the acetabular level. The bowel most often lies more superiorly in the child. When the rectogenital pouch is abnormally deep, in young and middle-aged patients the inferior margin of bowel is near normal during relaxation but is depressed under straining. In elderly subjects, it lies very low without straining. Generally the inferior margin also changes from the normal inverted cone shape, through an equilateral configuration, to a pear-shaped outline. In 28 cases of defecation block subjected to laparotomy, these findings were confirmed. One case of true rectal prolapse is illustrated.

Twenty roentgenograms; 6 diagrams.

JOHN F. RIESSE, M.D.
Springfield, Ohio

Internal Fistulae of the Digestive System. H. Laux and H. J. Gombert. *Fortschr. a. d. Geb. d. Röntgenstrahlen* 78: 153-159, February 1953. (In German)

Internal fistulas are abnormal communications (1) between cavities of the body, (2) between internal hollow organs, (3) between a hollow organ and a body cavity, and (4) between a hollow organ and a preformed cavity, abscess, etc. Frequently the development of a fistula is unnoticed clinically; at other times alarming symptoms may appear.

Esophageal fistulas are usually due to esophageal or bronchial carcinoma.

Fistulas of the stomach may lead to the colon or to the small bowel, less frequently into the pleural cavity or bronchi. Diarrhea or fecal vomiting may accompany the condition. Cancer or peptic ulcer is the pri-

mary lesion. Ulcer perforation may also produce abscess formation in the pancreas or liver.

Fistulas of the gallbladder or bile ducts are usually due to perforation of a stone into the duodenum, colon, etc. The stone may wander into the small bowel or colon, with consequent mechanical ileus. [The abstracter has seen a case in which the fistula led to the duodenum and the perforated gallstone was pressed into the stomach through the pylorus (Radiol. clin. 10: 1, 1941).] Perforation of a gallstone into the urinary system is a rare curiosity.

Fistulas of the colon arise by perforation of a carcinoma or a diverticulum.

The mechanism of fistula formation frequently may be revealed only by meticulous roentgen examination.

Nine roentgenograms. LEWIS L. HAAS, M.D.
Chicago, Ill.

Cholecystography in Dystonia and Dyskinesia of the Gallbladder and Bile Passages. František Bilek. Acta radiol. et cancerol bohemoslov. 7: 19-28, 1953. (In Czechoslovakian, with English summary)

Disturbances in the function of the gallbladder and biliary passages may be manifest as dystonia, brought about by pressure changes in the ducts, and dyskinesia as a result of impaired emptying of the gallbladder. Such disturbances may be either functional or organic in origin. Underlying the former are "disturbed nervous correlation of the mechanism of evacuation, and pathological viscerovisceral and corticovisceral reflexes." The latter are due to mechanical causes, as congenital anomalies, inflammations, fibrosis, cholelithiasis, and tumors.

It is not always possible, on the basis of cholecystography alone, to determine the exact nature of a dyskinesia, but it is possible to indicate that group of cases in which supplementary laboratory procedures, such as duodenal probing, will afford a more accurate distinction.

The conclusion is reached that serial cholecystography checked by laboratory examination may be to a large extent a basis for more refined differential diagnosis of dyskinesias of the gallbladder and biliary passages.

One drawing; 1 table.

Obturation of the Duodenum as an Aid in Cholangiography. Morris C. Miller, William S. Blakemore, and Roderick L. Tondreau. Surgery 33: 60-64, January 1953.

The authors describe a procedure which permits more adequate visualization of the biliary radicles than does cholangiography as usually performed. A thin rubber balloon, 3 1/2 inches long, fitted over the distal end of an Abbott-Rawson tube, is introduced into the second portion of the duodenum under fluoroscopic guidance (any type of tube may be used provided its lumen has free communication with the balloon for the introduction or withdrawal of air). The balloon is inflated with sufficient air (about 75 ml.) to obturate the lumen of the duodenum, but not enough to give rise to the pain of excessive distention. A radiopaque material is then injected into the ductal system through the common duct tube, and roentgenograms are made in the usual manner.

Three cases are reported in which ordinary cholangiographic studies failed to yield the desired information due to unsatisfactory demonstration of the biliary

radicles. Sufficient pressure could not be built up in the biliary tree because the injected contrast medium escaped into the duodenum. Inflation of the balloon in the duodenum prevented the escape of the medium downward into the intestine and permitted it to fill the upper part of the biliary tree, thus producing adequate visualization.

Six roentgenograms; 1 photograph.

THE MUSCULOSKELETAL SYSTEM

The Familial Occurrence of Infantile Cortical Hyperostosis in Utero. William P. Barba, II, and Dick J. Freriks. J. Pediat. 42: 141-150, February 1953.

This report deals with the occurrence of infantile cortical hyperostosis in two siblings. The first infant had bony abnormalities in the arms and legs revealed in a roentgenogram taken a week before delivery. The postnatal roentgenograms showed cortical thickenings of the mandible, clavicles, radii, ulnae, several ribs, tibiae, and fibulae, limited to the diaphysis in the tubular bones. At birth, brawny, tender, non-hyperemic, fusiform swellings of both arms and legs, the mandible, clavicles, and two ribs were present. Various laboratory tests were normal except for an elevated alkaline phosphatase. No treatment was given other than the usual "well-baby" care. The course was severe and protracted until the age of seventeen months, at which time the abnormalities began to clear.

In the second child, born twenty-three months after the first, the disease involved only the right tibia. The bony abnormality was demonstrated roentgenologically *in utero* and again postnatally. ACTH was administered for one week, with marked improvement of the lesion.

In discussing the possible etiology of this disease, the authors disagree with Caffey's view that it represents an infection. Biopsies which have been obtained by others have not disclosed any evidence of inflammation. Endocrine dysfunction is also unlikely, since the epiphyses are not involved by the hyperostosis. The authors believe that some vascular abnormality is at the basis of what they term "embryonal osteodysgenesis."

Thirteen roentgenograms.

PAUL W. ROMAN, M.D.
Baltimore, Md.

"Puerperal Osteophytosis" of Rokitsky. Contribution to the Radiological Study of Cranial Changes in Pregnancy and the Puerperium. N. Ludovico and G. Collo. Ann. radiol. diag. 25: 476-486, 1952-53. (In Italian)

Rokitsky described endosteal plaques in the frontal bones, similar to those seen in old age, in about 50 per cent of skulls of gravid women at postmortem examination. The authors performed radiological examinations of the skulls of a series of 65 pregnant women and found this condition in 3. In each instance the new bone disappeared within several months after delivery. Eighteen cases of this series showed calcification of the falx and synostoses at the frontoparietal sutures, but because these findings are so common, and since they did not disappear within several months, the authors are not at all sure that they are related to the pregnancy, even though Rokitsky and others so considered them.

The term "puerperal osteophytosis" is inaccurate on two counts: (1) the condition is found not only in the

puerperium but also in the preceding pregnancy; (2) it is probably not a true osteophytosis, but rather "intratabular" new bone formation.

While there is some parallelism between this condition and the better known hyperostosis frontalis interna of Morgagni, found in post-menopausal females, there are certain differences: the new bone in the condition under discussion is in the posterior part of the frontal bone, its density is not great, its limits are more precise, and its presence is transitory, whereas the bone in Morgagni's hyperostosis is in the anterior part of the frontal bone, is more dense, its limits are less precise, and its presence is permanent.

There was nothing clinically in the 3 patients to point to the radiologic changes in the skull.

The cause of this condition is unknown, but it is probably related to the sex-hormonal changes incident to pregnancy, in addition to an individual predisposition.

Six roentgenograms.

CHRISTIAN V. CIMMINO, M.D.
Fredericksburg, Va.

Hypertrophic Osteoarthropathy in Pulmonary Malignancies. Edward S. Ray and Hugh P. Fisher, Jr. *Ann Int. Med.* 38: 239-246, February 1953.

The gross pathologic process in osteoarthropathy is essentially one of proliferative subperiosteal osteitis surrounding the shaft of the bone. The long bones (tibia, fibula, radius, ulna, femur, and humerus) are the ones primarily involved. In advanced cases there may be involvement, also, of the clavicle, rib, scapula, and vertebrae. Although, symptomatically, regression of the osteoarthropathy often occurs, in only a few cases is there roentgenographic evidence of resorption of the newly formed bone. Frequently a decrease in the soft-tissue swelling around the joints is seen as the primary disease improves.

Many theories exist as to the causative factors in pulmonary osteoarthropathy. None has satisfactorily explained this interesting phenomenon. The demonstration of the reversible nature of the condition, as noted in some cases following pulmonary resection, indicates that the underlying causative factor arises from the lungs.

The authors studied a series of 139 cases of carcinoma of the lung to determine whether any relationship exists between osteoarthropathy and the type and location of the pulmonary lesion. Among the 139 cases were 14 of acute pulmonary osteoarthropathy. In all of these, the initial complaint was referable to the painful joints. In 5 cases, however, cough developed within three months of the bone pains. The knees, ankles, elbows, wrists, and phalanges were about equally involved. In all cases, roentgenograms of the involved joints revealed periosteal changes characteristic of osteoarthropathy. Clubbing of the fingers was present in all.

With one exception, in this group of 14 cases the tumor was located peripherally. In 2 cases a major bronchus was secondarily involved. In each the primary tumor appeared to arise from a small bronchus and to have extended by continuity to the major bronchus. In no instance was the lesion visible bronchoscopically on first examination.

No apparent relation was noted between the type of the tumor cells and the osteoarthropathy. The series included: squamous-cell carcinoma, 8 cases; adeno-

carcinoma, 3 cases; undifferentiated, 1 case; rhabdomyosarcoma, 1 case; metastatic fibrosarcoma, 1 case. Nor was any relationship found between the size of the carcinoma and osteoarthropathy.

Each of the 139 cases was studied to determine whether infection played a part in the development of osteoarthropathy. Infection was obvious clinically and histologically in 57 cases; in 3 there were large abscesses present, and in 2 the carcinoma was in a lung cyst. In none of these cases was osteoarthropathy present, from which it is obvious that infection plays no significant role in the development of bone changes.

A review of the literature regarding hypertrophic osteoarthropathy in carcinoma of the lung showed a predominance of peripheral pulmonary lesions, as in the present series. As in the authors' cases, also, there was no indication of the predominance of any histopathologic type, although adenocarcinoma was about as frequently encountered as squamous-cell carcinoma.

Two roentgenograms; 14 diagrams.

STEPHEN N. TAGER, M.D.
Evansville, Ind.

The Syndrome of Scoliosis Associated with Enlarged Thymus. Megalothymic Scoliosis. G. Paltrinieri. *Ann. radiol. diag.* 25: 260-271, 1952-53. (In Italian)

The author describes a syndrome seen in infancy, consisting of scoliosis associated with thymic enlargement, with disappearance of the scoliosis following irradiation of the thymus. One case is described in some detail. An infant, two months old, showed a rather marked left-sided dorsolumbar scoliosis, with the fulcrum at D-12 and L-1. Six months following irradiation of the thymus the scoliosis had disappeared. Treatment consisted of 80 r per sitting, on alternate days, for a total of 240 r.

The syndrome occurs more frequently in males. The author proposes that the scoliosis is a compensatory respiratory mechanism offsetting the mild pressure effects of the enlarged thymus upon the bronchi, heart, and great vessels, the enlarged hemithorax being on the side opposite that which contains the greater amount of thymic tissue. It is not likely that this condition results from myasthenia gravis. Further observation will be necessary to confirm the author's conception of the pathogenesis.

These children presented no endocrine abnormalities, but some showed mild effects of a mediastinal mass, such as laryngeal stridor, slight cyanosis of the lips, etc. Treatment should be undertaken before the soft and bony tissue changes become irreversible.

Three roentgenograms.

CHRISTIAN V. CIMMINO, M.D.
Fredericksburg, Va.

Anterior Dislocation of First Cervical Vertebra Simulating Cerebral Birth Injury in Infancy. Eben Alexander, Jr., Richard Masland, and Carlton Harris. *Am. J. Dis. Child.* 85: 173-181, February 1953.

Because the pediatrician and the neurologist are often confronted with the handicapped child showing evidence of paralysis and exhibiting seizures of one form or another due to cerebral birth injury, such signs and symptoms due to other causes are likely to be overlooked. A clinical picture simulating cerebral injury can occur as a result of compression of the cervical cord,

which may be due (1) to tumors of the posterior fossa or cervical cord or to bony exostoses in this location; (2) to congenital anomalies in the region of the foramen magnum or the upper cervical spine, such as the Arnold-Chiari malformation or platybasia; (3) to infections of the pharynx resulting in dislocations of the upper cervical spine; (4) to traumatic dislocations and fractures of the upper cervical spine.

A single case report is presented of a 21-month-old child who had repeated seizures from the age of ten months. He began to walk at thirteen months but dragged the right foot, often striking it against the left. He used the left hand poorly. After the age of fifteen months his ability to walk deteriorated. He ceased to gain weight but his mental development was normal. On admission to the hospital, the child was acutely ill; he breathed irregularly, but was not cyanotic. There was no rigidity of the neck, and the head was of normal size. The extremities were moved only rarely and presented the appearance of extreme weakness. The deep tendon reflexes were equal and active, and sensation over the entire body was apparently intact. Roentgenograms of the cervical spine demonstrated forward displacement of the atlas on the axis, with an indistinct outline of the body of the atlas. Operation revealed a transverse indentation of the cervical cord immediately under the arch of the atlas, due to a dense constriction of the dura. The cerebellum was normal, and the cervical spinal cord both above and below the point of constriction was slightly swollen. The patient's condition was unimproved by the procedure and he died nine hours after operation. The findings described above were confirmed at autopsy.

The authors believe that the patient's symptoms were due to the chronic dislocation of the atlas on the axis, with compression and degeneration of the cervical cord. Further, they believe that an important clue to the non-cerebral origin of the disorder was the fact that the child continued to show entirely normal mental development and a high degree of alertness, though there was no question that the signs and symptoms in the early stage of the illness were those frequently seen in cerebral palsy.

The etiology of the malformation is not obvious and there is no history of trauma, though the occurrence of injury during delivery cannot be excluded. The fact that symptoms of lesions in this region are not infrequently delayed lends some support to this possibility. Finally the authors point out that roentgenograms of the skull and cervical spine in patients presenting the picture of seizures, paralysis, and physical retardation should be beneficial in revealing remediable lesions, as in this case, at a stage when therapy might be effective.

Two roentgenograms; 3 photographs; 1 drawing.

L. R. JAMES, M.D.
Boston, Mass.

The Value of Pantopaque Myelography in the Diagnosis of Herniation of the Nucleus Pulposus in the Lumbosacral Spine. A Report of 500 Cases. S. A. Leader and Marvin J. Russell. *Am. J. Roentgenol.* 69: 231-241, February 1953.

The authors report on a series of Pantopaque lumbar myelograms and analyze the myelographic, clinical, and surgical findings in 414 cases. The myelographic diagnosis was verified at operation in 356 cases, approximately 86 per cent, and was found to be in error in 58 cases (14 per cent). The errors are listed as follows:

8 negative myelograms in which herniated disks were found.

18 with myelographic defects but no herniated disks, including 4 with two myelographic defects.

9 with two myelographic defects in which a herniated disk was present at one level but not at the other.

9 with two myelographic defects in which a herniated disk was present at one level but no exploration of the other level was done.

4 with a myelographic defect at one level and a herniated disk at a different level.

6 with a myelographic defect in error as to the side of the lesion.

4 with equivocal myelograms. In 2 of these, herniated disks were found at surgery; in 1, no herniated disk was found; in 1, a herniated disk was found at one level but not at the other level suspected.

The clinical diagnosis was found to be correct in 265 cases, or 61.6 per cent of the series, although in 82 of this number the level of the lesion was not specified prior to myelography.

From these observations, it is concluded that myelography should be done in every case of suspected herniation of the nucleus pulposus. The procedure is not infallible, however, and a negative myelogram should not be taken as a contraindication to surgery in the presence of strong clinical evidence. Myelography is particularly valuable in accurately locating herniated disks, demonstrating cord tumors when clinical findings are inadequate, and showing multiple disk herniations and associated herniated disks and tumors. No untoward effects of the procedure were observed in this series.

Twenty-four roentgenograms; 1 table.

LAWRENCE A. DAVIS, M.D.
University of Louisville

Primary Tumors of the Frontal Bone. Hans Brunner. *Arch. Otolaryng.* 57: 158-172, February 1953.

Tumors of the frontal bone, especially those originating in the frontal sinus, are less frequently reported than tumors of the ethmoidomaxillary area. This the author attributes in part to the fact that in some persons there is no frontal sinus and in part to the frequent difficulty of the diagnosis. He reports two cases, one of hemangioma and one of osteogenic sarcoma.

In the case of hemangioma, the x-ray examination revealed normal sinuses but indicated a connection of the tumor with the diploic veins. Two veins from the left side took a convergent course toward the frontal sinus and ran apparently toward an area of rarefaction corresponding to a tumor on the patient's forehead. There was no periosteal reaction in this case, and for that reason no "sun-ray" pattern was demonstrable. Microscopically, the compact line of the external lamina had been replaced by spicules of bone scattered between the blood spaces and separated from the latter by loose connective tissue or by the endothelium of the blood vessels. The correct diagnosis was not made until after operation. Only then was the x-ray picture properly interpreted. Preoperatively, syphilitic periostitis and osteitis and non-specific periostitis of the frontal bone were considered. Cases of each of these diseases are reported to show the similarity of the x-ray findings in the several conditions.

In the case of osteogenic sarcoma, the most striking x-ray finding was a "tremendous amount" of new bone formation in the diploë and the sinus, obliterating the normal osseous markings and the sinus cavity. The diffuse sclerosis was more evident than the subperiosteal tumor growth. This is in sharp contrast to primary carcinoma of the frontal sinus, in which destruction of bone prevails, without formation of reactive bone. Diffuse sclerosis is not in itself, however, diagnostic of sarcoma, as this finding may occur in other conditions, particularly chronic osteomyelitis. Cases of carcinoma and osteomyelitis are briefly presented to illustrate the differential problem.

Nine roentgenograms; 3 photomicrographs; 1 drawing.

Roentgenologic and Clinical Aspects of Hyperphalangism (Polyphalangism) and Brachydactylism. Hereditary Abnormal Segmentation of the Hand. Melvin I. Shoul and Max Ritvo. *New England J. Med.* 248: 274-278, Feb. 12, 1953.

The authors present 3 cases of a rare congenital syndrome involving the hands and feet. Forty cases have previously been reported, chiefly in the French and German literature. The syndrome consists essentially of five anatomic features: hyperphalangism (polyphalangism), with four rather than three phalanges in the middle finger and sometimes the index finger; brachyphalangism or shortening of certain phalanges (the middle phalanx of each finger and toe is markedly shortened, being about a third the normal length); the proximal phalanx of the ring finger is abnormally long; the base of the proximal phalanx of the index finger articulates with the metacarpal head obliquely and deviates ulnarward; and in preadolescent patients there is an extra, roughly triangular bone at the base of the index finger that probably corresponds to the extra phalanx in the middle finger (this supernumerary bone usually fuses with the proximal phalanx during adolescence). The hand is grossly deformed, and the anomaly is obvious on casual examination.

The authors draw attention to the fact that it is inherited along Mendelian-dominant lines and is often accompanied by congenital anomalies in other parts of the body. The patients often have no interference with function.

Three roentgenograms; 3 photographs.

SEYMOUR A. KAUFMAN, M.D.
Boston, Mass.

THE SPINAL CORD

Neoplasms of Central Nervous System Simulating Degenerative Disease of Spinal Cord. H. R. Oberhill, Roger A. Smith, and Paul C. Bucy. *J.A.M.A.* 151: 612-619, Feb. 21, 1953.

Neoplastic involvement of the central nervous system is most commonly confused with multiple sclerosis or amyotrophic lateral sclerosis and, on occasion, in elderly people may simulate subacute combined degeneration of the spinal cord. Five cases are reported not only to demonstrate the imitation of degenerative disease by neoplastic lesions but also to call attention to the pitfalls and indicate how they may be avoided.

Certain common errors may contribute to the confusion existing between these conditions: (1) It has been held that a myelogram is not indicated in the absence of evidence of obstruction of the spinal subarach-

noid space on Queckenstedt's test. This has previously been shown to be false as regards herniated cervical intervertebral disks that compress the spinal cord. The present series of case reports shows it to be false, also, for intraspinal lesions. (2) Myelography, on the other hand, may fail to reveal the presence of a herniated mid-line disk or of an intraspinal tumor. (3) Pain and sensory change are so often associated with intraspinal tumors that they are sometimes considered essential to such a diagnosis. This is not the case. Space-occupying lesions lying anterior to the spinal cord are particularly likely to produce only motor symptoms, without sensory alterations, thus leading to confusion with amyotrophic lateral sclerosis or multiple sclerosis.

Further, it must be remembered that a negative roentgenogram of skull and spine is meaningless. The view may be of a wrong area, and it is always possible that changes may be seen in other views. Among the most valuable findings on examination of the vertebral column are widening of the spinal canal and erosion of the vertebral pedicles.

Ancillary evidence, such as the age of the patient, may be helpful in differentiating degenerative and neoplastic disease. It is known that multiple sclerosis is predominantly a disease of young adults, while amyotrophic lateral sclerosis occurs primarily in older people. When symptoms of either disease appear in a patient of inappropriate age, a careful investigation should be made to rule out compression of the spinal cord by tumor.

Finally, in every case in which signs of involvement of the spinal cord can be explained by a single well localized lesion but without other evidences of an intraspinal tumor, the advisability of an exploratory laminectomy must be seriously considered. If there exists a real possibility of a space-occupying lesion compressing the spinal cord, it is better to err on the side of seemingly unnecessary exploration than to leave a remediable lesion untreated.

Six roentgenograms; 1 drawing; 1 graph.

L. R. JAMES, M.D.
Boston, Mass.

Myelographic Demonstration of Spinal Cord Metastases from Primary Brain Tumors. Ernest H. Wood, Juan M. Taveras, and J. Lawrence Pool. *Am. J. Roentgenol.* 69: 221-230, February 1953.

There is increasing evidence that metastasis of brain tumors to other portions of the nervous system by way of the cerebrospinal fluid is a relatively common occurrence. The authors believe that myelography is an excellent means of detecting these spinal metastases and determining the effect of roentgen therapy upon them. The frequent occurrence of spinal metastases from medulloblastoma is well recognized, but the frequency of such metastases from other gliomata is less well known. Ordinarily the metastases are not disclosed on the plain roentgenograms of the spine. Occasionally, however, the gravitation into the spinal canal of hemostatic clots used in brain surgery may indicate the occurrence of tumor.

The authors present 4 cases, 2 of cerebral glioblastoma multiforme and two of cerebellar tumors, all of which showed metastases in the spine. In all 4 cases myelography disclosed multiple filling defects in the contrast outline of the subarachnoid space. The defects appeared as rounded areas of diminished

density, and these defects were reproducible. The metastases may cause complete obstruction to the flow of the opaque medium. The spinal cord is usually not displaced, since the multiplicity of the metastases prevents shift in any one direction.

In one case myelography before and after radiation therapy to the spine afforded excellent indication of the efficacy of the treatment.

Nine roentgenograms; 2 photographs.

LAWRENCE A. DAVIS, M.D.
University of Louisville

THE GENITOURINARY SYSTEM

The Late Results of Ureterocolic Anastomosis. Arthur Jacobs and W. Barr Stirling. *Brit. J. Urol.* 24: 259-290, December 1952.

As a part of the study on the late results of ureterocolic anastomosis reported here, the authors made roentgen observations pertaining to the regurgitation of air and bowel content up the ureter into the kidney. Pneumopyelograms were demonstrated in nearly 50 per cent of patients following direct anastomosis, while only about 8 per cent of those in whom the indirect method had been used showed air in the upper urinary tract. A radiopaque medium instilled into the bowel was demonstrated in the ureter in about a third of the cases of direct anastomosis but in none of those with indirect or oblique anastomoses.

This higher incidence of reflux from the bowel is not, however, considered a contraindication to direct anastomosis, since no unfavorable clinical effects have been observed and since the postoperative renal status of the direct implants, as judged by urographic studies, has proved superior to that of those done by the indirect technique.

This paper is a long one, based upon a collective survey including 1,673 cases in which ureterocolic anastomosis was done, as reported, in response to a questionnaire, by 137 surgeons. It deals at length with the indications for the procedure, its results in various conditions, the complications, and the blood electrolyte changes following operation. The need of adequate follow-up examinations including biochemical and roentgen studies is stressed.

The text is illustrated by 10 roentgenograms and a large number of graphs. An appendix (pp. 290-304) contains an elaborate tabulation of the data (compiled by W. B. Fletcher) upon which the study was based.

THE BLOOD VESSELS

Pathogenic Study of Varicose Veins. P. Piulachs and F. Vidal-Barraquer. *Angiology* 4: 59-100, February 1953.

The authors have made a comprehensive study of four groups of cases, as follows: idiopathic varicose veins, 92 cases; varicose veins of pregnancy, 21 cases; postphlebitic varicose veins, 30 cases; congenital arteriovenous fistulas, 14 cases. The methods of examination employed included serial arteriography, retrograde phlebography, determination of the oxygen content of the varicose blood, determination of femoral artery-tongue time, and anatomopathologic study of dilated veins. As a result, the conclusion is reached that all varicose veins, whether idiopathic or postphlebitic, have a common initial pathogenesis, originating through the existence of numerous small congenital

arteriovenous channels which are universally present in a functionally latent state and suddenly become active through the action of a "starting agent."

This view is supported by clinical observations, by the pronounced reduction of the femoral artery-tongue time observed in all the idiopathic cases, by increase of oxygen saturation in the varicose blood, by studies of dissected varicose vessels, and by roentgenologic observations.

Serial arteriograms were obtained in 38 cases of idiopathic varicose veins as well as in a group of normal subjects. Even in the latter, evidence was found of telangiectasia, phlebectasia, and bulging—though not actually varicose—veins. In the varicose group the serial views demonstrated rapid passage of the opaque medium into the venous system, with absence of a distinct capillary phase, and in some instances actually showed the arteriovenous communications.

In 23 cases, retrograde phlebography was also performed to demonstrate the valvular competence or incompetence of the deep venous system. Valvular incompetence proved not to be a constant finding, occurring in only 13 of the 23 cases, thus ruling it out, in the authors' opinion, as a cause of idiopathic varicose veins.

Two factors are considered to be operative in the production of varices, a congenital factor and an exciting factor. As previously pointed out, arteriovenous communications are believed to be present to some degree in all persons. Usually they are small, few in number, and functionally latent. They may, however, be more numerous and of greater size, in which event dilatation as a result of some starting agent produces new hemodynamic conditions leading to further dilatation and eventually to varicose veins. Among the starting agents, or exciting factors, the authors mention hormonal disturbances (as in pregnancy), extreme heat, and trauma, including the microtrauma incident to prolonged standing.

A special study of 21 patients with postphlebitic varices showed these also to be due to the pathological process of arterial shunts in the form of congenital arteriovenous fistulas. The development of a deep thrombosis is an obstacle to the venous blood flow since, beside the reflex disturbances it induces, it also brings about a mechanical disorder in the circulation. This results in dilatation of the congenital arteriovenous channels, which in turn promotes the return of the blood flow hampered by the thrombosis, since a portion of the arterial blood is directed into the patent veins. This leads to the creation of numerous arteriovenous fistulas which, on account of carrying the blood into the veins at a higher pressure, turn these vessels into varicosities.

Therapeutic measures are briefly mentioned. They consist in suppression of varicosities and of arteriovenous channels and the correction of valvular incompetence of the deep venous system.

Forty-four arteriograms and phlebograms, with accompanying drawings; 16 photographs and photomicrographs.

The Actions of Intra-Arterial Diodrast, Thorotrast, and Sodium Iodide on the Peripheral Pulse Volume of the Lower Extremity. R. P. Jepson and F. A. Simeone. *Surgery* 33: 276-283, February 1953.

The complications which follow the intra-arterial use of contrast media include, beside the familiar

"toxic" or "sensitivity" reactions, those due to the arterial puncture and those attributable to the irritative action of the medium in the limb. The most severe of the limb sequelae is local or massive tissue necrosis, which has frequently been attributed to a vasospasm and subsequent arterial thrombosis thought to be induced by the contrast agent.

The authors report a study on dogs and in man to determine if a severe and persistent vasospasm did in fact occur after the introduction of certain contrast media into the arteries of the lower extremities. Pulse volume recordings were made with an electroplethysmograph following the injection of 35 and 70 per cent Diodrast, 10 per cent sodium iodide, and Thorotrast into the femoral artery of nine dogs. Similar recordings following the injection of 35 per cent Diodrast into the femoral artery were made in 3 patients. In dogs, either no change in pulse volume occurred or a vasodilatation resulted, with or without a brief period of vasoconstriction. Vasodilatation was also observed following the arterial injection of such innocuous substances as isotonic saline and buffered phosphate solutions.

In none of the 3 patients was vasodilatation observed. In 1 extremely nervous patient there was a rather marked vasoconstriction, with return of the pulse wave to the pre-injection level after eight minutes. In the other 2 there was either no diminution of the pulse volume or a brief incomplete vasoconstriction with recovery in two minutes.

From these observations it is concluded that the vasoconstriction resulting from the injection of Diodrast is insufficient to account for the occasional femoral artery thrombosis reported in the literature. It is suggested that intimal trauma and traumatic arteriospasm, especially in the diseased artery, are the more likely explanations.

Six electroplethysmographic recordings.

Hepatic Venography in Man. G. Tori. *Acta radiol.* 39: 89-97, February 1953.

The author presents a method of visualization of the hepatic efferent venous system in living human subjects. The technic was suggested by Rappaport's application of a similar procedure in dogs (*Acta radiol.* 36: 165, 1951. *Abst. in Radiology* 59: 148, 1952).

The procedure is to be distinguished from hepatic arteriography by means of aortography, portal venography by direct injection at laparotomy, and portal venography by splenic puncture. A catheter (generally a Courmand 9-12) is introduced into the right auricle by the usual catheterization technic but, instead of the tip being pushed through into the ventricle, it is, by means of axial torsion, directed posteriorly and, in contact with the posterior auricular wall, is advanced into the inferior vena cava. At about 2 or 3 cm. below the diaphragm, the openings of the hepatic veins are presumed to be reached. Still under fluoroscopy the catheter is rotated either to the right or left for entrance into the hepatic vein selected. The right branches are more easily entered because of their larger size; the left less readily because of a narrower lumen and because they divide immediately. Visualization is obtained by injection of 20 to 25 c.c. of 70 per cent Diodrast given at the rate of 4 or 5 c.c. per second. Films are made with the patient supine, and two or three are usually obtained at intervals of one or two seconds while respiration is suspended.

The method has been used on 10 patients, who showed an excellent tolerance to the procedure. Two pathologic cases were studied; the others were normal. In one case of knobby liver and suspected neoplasm, the medium was introduced into the main right trunk but was blocked after filling of about 8 cm. and only a few secondary branches were filled. These were displaced at right angles, presumably by the growth. In the second case, myeloid leukemia, injection of the left superior group revealed a configuration described as "obviously different from the normal," though in what respect is not explained.

During contrast filling of the hepatic veins a common occurrence was the appearance of extensive opaque blotches in the adjacent area. The author believes that these are best explained by the peculiarities of the efferent drainage system of the liver. Besides the main vein trunks, which make up the superior hepatic veins, there are a variable number of small veins which open by means of minute orifices lying inferiorly to the larger veins, and these comprise the inferior group. In addition, small confluent vessels enter the larger veins even near the vena cava. The catheter tip, lying against the wall, may obliterate one or more vessels and thus produce an increase in local pressure which will cause contrast medium to be diffused successively into intralobular veins and sinusoids.

The author has no definite opinion on the practical possibilities of the method at this time. Its application in a larger number of cases will indicate its value.

Six roentgenograms with diagrammatic drawings; 1 sketch.

JOHN F. RIESER, M.D.
Springfield, Ohio

TECHNIC

On the Visualization of Ulcerative Processes Using Hydrogen Peroxide in the Contrast Medium. A Preliminary Report. Paavo Klami. *Acta radiol.* 39: 98-104, February 1953.

Hemoglobin will break down hydrogen peroxide into oxygen with liberation of other substances. Likewise, leukocytes will reduce hydrogen peroxide into its elements. As a result, when an ulcer bathed in pus is cleansed with hydrogen peroxide, there is marked formation of foam. This property of hydrogen peroxide is suggested for practical application during roentgen examination for the differential diagnosis between cicatricial and ulcerative lesions.

An ordinary barium sulfate preparation mixed with 3 per cent hydrogen peroxide in water was used as a contrast medium. If all blood and pus has been removed by lavage from the general area of examination, foam is expected to be demonstrated where an ulcerative process is situated.

Approximately 40 examinations were conducted on proved cases of ulcerated lesions, both benign and malignant, and on cicatricial lesions, as well as in normal persons. Marked foam formation was noted in several cases of hemorrhagic gastritis. Ulcerated carcinomas of the lower esophagus and stomach showed foam formation. One case of obvious carcinoma of the stomach did not show foam, but it was not proved whether ulceration was present. The foam appears to be rather easily recognized on films.

The method would appear to be of more value in examination of the esophagus than of the stomach. In theory it could be adapted to retrograde study of the

kidney, but at present this is impossible, since current pyelographic media contain organic iodine compounds which do not permit the addition of hydrogen peroxide.

Ten brief case reports are included.

Thirteen roentgenograms.

JOHN F. RIESSER, M.D.
Springfield, Ohio

A Simple Method of Relative or Absolute Roentgen Planimetry. D. Schoen and H. E. Magnus. *Fortschr. a. d. Geb. d. Röntgenstrahlen* 78: 196-204, February 1953. (In German)

A method is described to simplify the determination of roentgen sizes of specific areas. A transparent millimeter graph paper is inserted between the intensify-

ing screen and the film. The divisions are visible on the exposed and developed films. The number of squares can be counted directly on the film, without intermediate contour drawing. Regression and progression of a lesion may be followed by these rapid measurements. The method is applicable to pulmonary cavities, contraction of the gallbladder, ulcer craters, the optic foramina, and the sella turcica area.

If the real depth of the measured area in the body is known, e.g., that of the sella, areas on tomograms, the factor of enlargement, and the actual size can also be calculated.

Eight roentgenograms; 7 graphs.

LEWIS L. HAAS, M.D.
Chicago, Ill.

RADIOTHERAPY

Carcinoma of the Eyelids. Bertil Roseberg. *Am. J. Roentgenol.* 69: 196-207, February 1953.

The author reports on the results of the treatment of 131 patients with 133 carcinomas of the eyelid seen at the State University Hospital, Iowa City, Iowa, from 1930 to 1943. Four general methods of irradiation were used and in some cases were combined with surgery. The largest group received intermediate roentgen therapy with total doses ranging from 800 to 2,000 r at one sitting or 2,000 to 5,000 r in fractionated doses. Another group was given low-voltage, short-distance therapy with single doses of 1,500 to 3,000 r for small lesions and divided doses of 500 r daily to a total dose of 6,000 to 7,000 r in ten to fourteen days for larger ones. In certain of the earlier lesions radium plaques were used and in a few, deep therapy. One hundred and two lesions were adequately surveyed for three years or longer. Of these, 85 per cent were healed after three years. The greatest percentage of healed lesions occurred in the group treated with low-voltage, short-distance therapy. The worst results were obtained with the use of radium.

Of 72 cases proved histopathologically, 54 were basal cell, 10 squamous-cell, and 8 intermediate-cell carcinomas. There was excellent response of those lesions which had been treated prior to irradiation with other means. When further treatment was required, those lesions having received intermediate or deep therapy in the beginning gave the best response. Those which had been treated primarily with low-voltage short-distance therapy responded poorly.

Of the total of 66 lesions treated with a single course of roentgen therapy, 63 were healed. Lesions located in the lateral canthus responded best, while lesions of the upper and lower lids gave the poorest response.

In addition to this analysis, the author presents a rather complete review of the literature on the subject.

Eight tables. LAWRENCE A. DAVIS, M.D.
University of Louisville

Cancer of the Breast. A Review. D. W. Smithers, P. Rigby-Jones, D. A. G. Galton, and P. M. Payne. *Brit. J. Radiol.* Supplement No. 4, 1952.

The authors have made a comprehensive review of cancer of the breast based on their extensive experience at the Royal Cancer Hospital. All the important factors related to the disease are covered. Results of treatment are accurately reported and development of a

treatment policy based on personal experience and that of others is presented. Tables and graphs are copiously supplied to simplify the conclusions reached, and the pertinent literature on the subject is quoted freely to support the contentions offered. Statistics are given which comprise all cases from 1937 through 1948.

The authors started collecting data in 1937 because they believed that there were a number of what appeared to be quite simple questions to which they could find no satisfactory answer. They undertook this study in an attempt to clarify their own ideas and now present the result in the belief that the time has come once more when a general review may be of interest to others.

The material consisted of 1,777 new patients, 1,762 women and 15 men, of whom 1,708 were treated and 69 were not. The absolute survival rate given for 1,093 patients treated at the Royal Cancer Hospital is 34.6 per cent, which compares favorably with results from other centers treating large numbers of patients with cancer of the breast. The survival rates according to stages varies considerably from center to center due to lack of uniformity of classification.

The conclusions drawn by the authors from their detailed studies are as follows:

Part I. Predisposing Factors: There is a steady downward trend in the mortality rate from breast cancer in England and Wales, after correction for changes in the age distribution of the female population; approximately 3 in every 100 women who reach the age of forty years may at present expect to die from this disease. The hereditary influences in the development of human breast cancer are complex in action, but, like similar inherited tendencies in mice, would seem to be specific for cancer at this site rather than general for malignant disease as a whole.

Social class and occupation have, in themselves, no demonstrable effect upon the incidence of the disease but are often linked with such significant factors as child-bearing, breast-feeding, and nutrition.

The state of *hormone balance* over long periods plays a part in the development of breast cancer. No definite variations in the age of onset or cessation of menstruation or the total duration of menstrual life have been established between those who do and those who do not develop this disease. The excessive production or diminished excretion of estrogens, from whatever cause, may play some part, as may the prolonged administra-

tion of estrogens therapeutically in rare cases. Further study is necessary to find out whether castration in early life affords some protection against the later development of breast cancer.

Cystic hyperplasia is commonly associated with breast cancer, but the more significant pathological changes are seldom the more obvious clinically. Cancer of multicentric origin in one breast and bilateral primary breast tumors are quite frequently found.

The uneven site distribution of primary breast cancers has not been satisfactorily explained; it may be due to no more than the relative amounts of breast tissue present but might bear some relationship to trauma among other factors.

The incidence of breast cancer is higher in single than in married women. It seems that the *marital status* and *parity* play a part. Lower birth rates predispose to higher incidence. There is no evidence on which to assess the likelihood of a non-genic hereditary *milk factor* in the production of human breast cancer in breast-fed children, but there is some to suggest that failure to breast-feed children may predispose to the development of the disease in the mother.

Part II. Factors Influencing Prognosis: The most important consideration in assessing the prognosis for patients with carcinoma of the breast is the *stage of advancement of the disease* at the time of first treatment. While this is related to the intelligence and temperament of the patient and the good sense and initiative of the doctor, it is largely dependent on the *rate of growth* and tendency to dissemination of the tumor, that is, to its degree of malignancy, which is linked to its *histological grade*. In other words, the most important factor in prognosis in patients with breast cancer is the character of the tumors they develop.

Duration of symptoms is important for the patients with the more active tumors, and the prognosis becomes rapidly worse for durations longer than three months. It is of less importance for patients with the more slowly growing tumors, and some of them, with a history longer than the normal expectation of life of others with untreated active tumors, may survive for many years.

Tumors developing during *pregnancy and lactation* are especially serious, since their activity tends to be high, but an occasional tumor with low activity does occur in this group, and these patients may then be treated successfully. Patients who have been successfully treated for breast cancer and show no sign of recurrence for three years or more may then sometimes pass through one or more pregnancies without ill effect.

There is no good evidence that the activity of breast tumors varies greatly with *age*, the slight variation that may exist is offset by other factors, so that the prognosis is comparatively good in the young, is worse in the *post-menopausal* group, improves again in the sixties and seventies, and worsens once more in old age.

Patients with tumors in the *inner half of the breast* have a worse prognosis than those with tumors in the outer half, the better clinical stage distribution of inner-half tumors being illusory and their treatment less efficient.

It is difficult to be certain that *trauma* has played a part in increasing the rate of growth of a primary tumor, but there is little doubt that it may influence the development of metastases.

Part III. Results of Treatment: If any real benefit is to be gained from reviews of the results obtained

in the treatment of breast cancer, much more care and uniformity in recording and presenting data must be achieved. Important factors other than treatment which influence the prognosis must be taken into account, especially the degree of activity of the tumors, the *stage distribution* of the material, the *methods of selection*, and the *years during which the patients were treated*. International agreement on methods of staging and of presentation of results is required.

No results should be presented which do not give the total number of new patients seen with the disease during the period concerned, whether treated or not treated at the hospital or sent for treatment elsewhere. The absolute survival rate on this total group, *all patients lost sight of being regarded as dead*, should always be stated before any subgroups are considered or any special statistical methods applied. The survival rates should be given for annual intervals and not only at five years, and "recurrence-free" rates should be stated as well.

Comparison of overall results obtained in the best treatment centers which do provide the basic data on which absolute survival rates can be calculated show that a steady improvement has occurred over the years but do not yet provide conclusive evidence that the slight differences observed in groups treated at about the same time are due to the treatment methods advocated and not to variations in the material treated. When the results are broken down into groups, a number of interesting suggestions appear, and it is greatly to be regretted that lack of uniformity in staging and presentation make it difficult to draw reliable conclusions.

Part IV. Development of a Treatment Policy: There would be less difficulty in deciding on the best method of treatment for each patient with cancer of the breast if we knew the exact limits of spread of the disease and the degree of malignancy of the tumor. There are only a number of indirect methods of gauging the former and the present methods of assessing the latter are only to be relied on after the breast has been removed, though the information is required before. It is possible that radioactive isotope studies may one day provide evidence as to extent and direction of spread and also degree of tumor activity. A notable advance in prescribing treatment would result if this were so.

Operation on the primary, and almost certainly on the axillary nodes as well, is more effective than radiotherapy in eradicating the disease, but radiotherapy does eradicate it in a proportion of cases and, in the event of failure to eradicate, delays its progress, whereas unsuccessful surgery tends to make matters worse.

Stricter criteria of operability for *radical mastectomy*, improved *radiotherapy* combined with local mastectomy, and preoperative irradiation combined with radical mastectomy have all tended to improve the survival rate. Further developments based on an estimation of the prognosis in each patient and the selection of the treatment method best suited to her needs might improve the absolute survival rate to 75 per cent for Stages I and II and 25 per cent for Stages III and IV, which is about 50 per cent for all patients seen with the stage distribution with which we are usually presented today. *Hormone therapy* and castration are sometimes valuable aids to palliation and may also help by gaining time for other treatments in the later stages of the disease.

Much of the improvement in results taking place in

many of the larger treatment centers is due to the fact that more patients are coming for treatment while still in a comparatively early stage of the disease. In a few it is due to the selection of an increasing proportion of those patients whose tumors are of a less active character. If 75 per cent of all patients with breast cancer were treated while still in Stages I and II, the absolute five-year survival rate for all the patients seen with this disease might be raised to over 60 per cent merely by employing to the best advantage the treatment methods already available. This may not be as easy to achieve as some propagandists believe, since the stage of the disease when the patient is first seen depends so much on the nature of the tumor and its degree of malignancy, which are not susceptible to educational programs.

Twenty-six figures: 61 tables.

HARRY HAUSER, M.D.
Cleveland City Hospital

Management of Carcinoma of the Uterus. Herbert E. Schmitz and Chester J. Gajewski. *S. Clin. North America* 33: 259-268, February 1953.

In considering the problem of pre-invasive carcinoma (carcinoma in situ) of the cervix, the authors feel that conservative therapy such as cauterization, conization, or amputation of the cervix is permissible in young women desirous of reproducing, provided the atypical cells have not invaded the lymph nodes. If the lymph nodes are involved, progression of the disease is likely. Under these circumstances, it is the authors' policy to remove the entire uterus but to preserve the gonadal function. If an intraepithelial carcinoma is found during pregnancy, vaginal delivery is permitted and treatment, as indicated, is then carried out. In patients in the fourth and fifth decades, the scope of the surgery is increased to include removal of pelvic lymphatics, parametrial tissues, uterus, upper third of the vagina, and both tubes and ovaries.

In invasive carcinoma of the cervix the primary method of therapy should be irradiation. The importance of attempting to detect the early irradiation failures so that surgery may be carried out before extensive fibrosis has developed, is stressed.

In patients with far advanced or recurrent carcinoma resistant to irradiation, the authors feel that the extirpation operation is indicated in certain carefully selected cases. They discuss some of their criteria used in selection of cases.

Endometrial carcinoma is treated by means of pre-operative radium in the Y applicator of Schmitz (up to 6,000 mg. hr.) and external x-ray irradiation (1,000 kv.) up to a level of 4,000 r in the mid-pelvic area. With this technic, no malignant cells remained in the uterus at the time of complete hysterectomy (six to eight weeks later) in 75.6 per cent of the cases. Even in those patients who do show residual tumor cells, there are changes in the cells, nodes, and blood vessels which suggest that these cells would have difficulty in surviving if implanted in the operative field or carried off through the vascular or lymphatic channels.

DEAN W. GEHEBER, M.D.
Baton Rouge, La.

Adenocarcinoma of the Uterine Corpus. Charles P. McCartney. *S. Clin. North America* 33: 241-257, February 1953.

The author states that carcinomas of the corpus con-

stituted 32.2 per cent of a series of malignant uterine tumors from the Chicago Lying-in Hospital and 23.4 per cent of all malignant lesions of the female reproductive tract. Fortunately, the rate of growth is slow, and in this series 77.6 per cent of the tumors were confined to the body of the uterus. In these cases, the five-year survival rate was 72.5 per cent. In the 22.4 per cent of cases which had spread beyond the uterine confines, the five-year survival rate was 2.64 per cent.

Irradiation therapy alone was used in 28 per cent of the patients, surgery being precluded by the general medical status. Most of this group were treated by Heyman's method of packing multiple radium foci into the uterus, although in some instances external x-ray therapy was also used. The survival rate in this specific group was 57.2 per cent.

Definitive surgery was feasible from medical and technical standpoints in 61 per cent of the series, and a wide excision was carried out. This included removal of the adnexa and excision of 2 cm. of vaginal cuff. Surgery alone was the primary form of therapy in 37.6 per cent of the patients, while 22.3 per cent were treated by radium preoperatively. In those cases in which the malignant growth was confined to the body of the uterus, primary surgery resulted in a five-year survival rate of 85.6 per cent. The combined method of therapy was attended by in an 83.5 per cent five-year survival rate.

In 43 per cent of the cases in which preoperative radium therapy was used, the surgical specimens presented no gross or microscopic evidence of malignant disease (surgery six to eight weeks after irradiation). In this group, the five-year survival rate was 100 per cent. In 14 per cent, the adenocarcinoma had persisted, but was still confined to the endometrium. In this group also, the five-year survival rate was 100 per cent. In 43 per cent of the combined group, the myometrium was involved and the five-year survival rate dropped to 63.5 per cent.

[The percentages as given in this paper would have more significance if the number of cases was stated. Nowhere in the course of the paper is there any indication of this.—Ed.]

Eight tables.

DEAN W. GEHEBER, M.D.
Baton Rouge, La.

The Prognostic Importance of the Gross Morphology of Carcinoma of the Uterine Cervix. Ulf Borell. *Acta radiol.* 39: 141-160, February 1953.

From 1914 to 1941, there were 4,611 patients with carcinoma of the uterine cervix referred to Radiumhemmet (Stockholm) for treatment. All case records were carefully studied, but for the investigation reported here only those cases were chosen in which there was a description of the gross morphology sufficient to allow accurate classification of the primary growth. This series totals 2,794 cases. The majority were examined by Professor J. Heyman and the extent and appearance of the growth were fully described.

The cases are divided into three groups:

1. *Exophytic* or *evert*ing tumor, usually a cauliflower growth. These may be very large and fill the entire vagina, are often soft to the touch, and microscopically are quite vascular and show scant connective tissue.

2. *Endophytic* or *invert*ing tumor, growing in the form of a disk beneath the cervical mucosa. Ulceration does not occur until late and then generally involves only

portions of the surface of the growth. The tumors are often very hard to the touch. They contain much connective tissue and few blood vessels.

3. *Crateriform* carcinoma. This type may arise from a tumor primarily either exophytic or endophytic.

The patients constituting this series were treated by radium combined with roentgen irradiation, according to the Stockholm method.

The results of this investigation are given as follows:

1. Endophytic and crateriform carcinomata were three to four times more common than those of the cauliflower type.

2. In the majority of the cauliflower tumors the growth was in Stage I or II (League of Nations classification) when the patient presented herself for examination, while most cases of the other two types were in Stage III or IV.

3. Cauliflower carcinoma was more common in young women, while the others occurred more frequently in older age groups.

4. The length of the history was practically the same in all three types, but it was suggested that the interval between the appearance of symptoms and first examination was shorter in the exophytic cases than in endophytic tumors.

5. The prognosis for exophytic tumors was better than for endophytic tumors, but the difference was appreciable only in cases of clinical Stage II.

The author discusses the defects in the classification used here. Eversion and inversion may occur at the same time in the same tumor. Transitional forms of growth are difficult to classify. Differential diagnosis between an ulcerating endophytic tumor and a crateriform lesion is extremely difficult at times. Some tumors may show characteristics of all three types.

The apparently significant finding in this study is the 39.7 per cent five-year survival in Stage II exophytic lesions compared with 27.3 per cent and 23.8 per cent in the endophytic and crateriform Stage II lesions, respectively. This suggests to the author that the cauliflower type has biologic characteristics other than its manner of growth as determined by vaginal examination which have a bearing on the end results.

Seventeen graphs; 7 tables.

JOHN F. RIESSE, M.D.
Springfield, Ohio

Transvaginal Cone Roentgen Irradiation in Cancer of the Cervix Uteri. Report of Twelve Years' Experience. John Y. Howson, Bernard P. Widmann, and James L. Weatherwax. *Am. J. Roentgenol.* 69: 182-189, February 1953.

In 1938, the use of transvaginal roentgen therapy was initiated at the Philadelphia General Hospital as a possible additional palliative adjunct in the treatment of advanced cervical cancer. The treatment plan includes preliminary high-voltage roentgen irradiation, consisting of a series of 2,000 r (in air) delivered through four skin portals 15×20 cm., with the rays directed to the tumor area, and a course of 8,000 to 12,000 r (air) administered through a vaginal cone to the tumor. The majority of cases receive the external therapy first, though in some cases the order is reversed and in some (especially in younger patients) the two procedures are conducted simultaneously. The external irradiation is done on alternate days, 150 r to each field until the ultimate tumor dosage of 2,000 r

(air) has been reached. Intravaginal treatment is given three times a week with the distal end of the vaginal cone directly over the cervix, 500 r (air) being delivered at a single treatment.

Up to Dec. 31, 1950, 361 patients had been treated, and of these 225 had received at least two courses of high-voltage irradiation through four external ports and at least one course of high-voltage radiation transvaginally. It is this group of 225 cases that forms the basis of this study. All stages are included, but the number of Stage I lesions is too small to be of significance.

A comparison of the results with previous series in which other technics were employed showed that the average duration of life was increased tremendously over that effected by external irradiation alone and to a lesser degree over that obtained with external irradiation plus radium. The clinical improvement in patients receiving intravaginal roentgen therapy is described as "most gratifying." Local regression of the lesion with control of hemorrhage and discharge was a frequent observation. Increased appetite and weight gain, decrease in pain, and an overall sense of well-being were almost constant findings except in the most advanced cases. The incidence of post-therapy complications, such as intestinal obstruction and fistulas, was low.

The authors conclude that, in view of the symptomatic relief achieved in this series, the regression of the local lesion, the low incidence of unfavorable reactions and sequelae, and the increased longevity in cases of Stages II, III, and IV, roentgen radiation delivered transvaginally should be used to supplement the conventional modes of administration of roentgen rays and radon in carcinoma of the cervix.

Four tables.

THOMAS E. PADGETT, M.D.
Louisville General Hospital

A Twenty-Year Study of Radiological Treatment of Cancer of the Cervix at the Montreal General and Royal Victoria Hospitals. Eleanor Percival. *Am. J. Obst. & Gynec.* 65: 386-389, February 1953.

The results of twenty years of radiological treatment of carcinoma of the cervix at the Royal Victoria and Montreal General Hospitals, 1927-46 inclusive, are presented. From 1920-25, when most clinics turned from surgical to radiological treatment of cancer, to the present time there has been a steady increase in the number of cases salvaged.

This series has been divided into two ten-year periods, 1927-36 and 1937-46. It comprises 1,200 cases of invasive cancer of the cervix, 506 from Montreal General Hospital and 694 from the Royal Victoria Maternity Clinic.

In Stage I and Stage II and in most Stage III cases, the treatment consisted of two radium applications given at ten-day intervals, followed by a series of deep x-ray treatments. An intra-uterine tandem of two 25-mg. tubes of radium (screened by 2-mm. brass and 3-mm. rubber) with three 25-mg. tubes in the vagina, one placed against the cervix and one in each lateral fornix, was the basic radium treatment, though it was often modified to suit the individual patient. The dose at the first treatment was 2,500 mg. hr.; at the second treatment 2,000 to 3,500 mg. hr. was given, making a total dose of 4,500 to 6,000 mg. hr. Usually both radium treatments were given before deep x-ray therapy. In Stage IV cases, roentgen irradiation

was used as a palliative measure. In the few Stage IV cases which showed an unexpected response, radium was applied cautiously at the end of deep x-ray therapy. Interstitial radium was not used.

X-ray therapy was administered through four ports of 150 sq. cm. each, the factors being 200 kv. and 0.5 mm. of copper, to give a total dose of 1,750 to 2,250 r measured in air, or 1,800 to 2,300 r against the lateral pelvic wall, which is calculated to be 5 cm. lateral to the internal os of the cervix.

The results of the treatment are divided as to the various stages and the two ten-year periods and are presented in table form.

A comparison of the 1927-36 period with the 1937-46 period shows an increase of the five-year "cures" as follows: in Stage I from 71.4 to 73.3 per cent; in Stage II from 51.0 to 60.1 per cent; in Stage III from 25.1 to 35.3 per cent. In Stage IV there was a decrease from 9.4 to 4.1 per cent.

The author discusses the reasons for the better results in the more recent years and concludes that the key-stone of treatment for cancer of the cervix today must continue to be radiation.

Five tables.

JOHN M. KOHL, M.D.
Jefferson Medical College

Primary Carcinoma of the Vagina. A Report of Forty-six Cases. Melvin D. Bivens. *Am. J. Obst. & Gynec.* 65: 390-399, February 1953.

At the University of Michigan Hospital, the incidence of primary vaginal carcinoma was 1.5 per cent of malignant tumors involving the female genital tract. The present report covers the period from 1931 through 1950. For every case of primary vaginal carcinoma there were 44 carcinomas of the cervix, 9 of the endometrium, 5 of the ovary, and 3 of the vulva.

The patients ranged from fifteen to eighty-three years in age with an average of sixty-four. The case of the fifteen-year-old patient is presented in detail. The group included 43 white women, 2 Negroes, and 1 Mexican. All but 2 were married or had been married. Five were nulliparous. Thirty-five patients had ceased to menstruate prior to the onset of symptoms associated with the vaginal carcinoma. Five of these had an artificial menopause, 3 by surgical procedures and 2 by x-ray castration. The average age of those who reached the menopause spontaneously was fifty-one years.

One patient, sixty-seven years of age, had worn a glass pessary for two and a half years without removing it; 2 patients had marked senile vaginitis.

Among 40 eligible cases there were 11 five-year survivals, or 27.5 per cent. The three-year, five-year, ten-year, and fifteen-year absolute survival rates are given in table form. The methods of treatment were (1) radium only, 4 cases; (2) x-rays only, 6 cases; (3) radium and x-rays, 28 cases; (4) local excision plus radiation, 6 cases; (5) radical surgery plus radiation, 1 case. One patient refused therapy.

There was no apparent correlation between the degree of anaplasia of the tumors and the five-year survival rate.

One graph; 3 photomicrographs; 8 tables.

JOHN M. KOHL, M.D.
Jefferson Medical College

X-Ray Therapy for Vesical Papillomatosis. Alan J. M. Nelson. *M. J. Australia* 1: 64-65, Jan. 17, 1953.

The author treated 5 cases of vesical papillomatosis with x-ray irradiation through three portals of 7.5 cm. diameter over the anterior abdominal wall and both buttocks, giving a total dose of 4,000 to 5,500 r in three to five weeks. The papillomas disappeared and for a time the bladder appeared normal and symptoms were absent. After one or two years, however, there were recurrences, which were almost as bad as the original lesions. Irradiation thus appears to be no better than simple fulguration in this condition.

The author postulates a similarity between bladder papillomas and verruca vulgaris.

PAUL MASSIK, M.D.
Quincy, Mass.

The Two Million Volt Van de Graaff Generator Installation Designed for Rotation Therapy at the Royal Cancer Hospital. B. M. Wheatley, P. R. Steed, E. W. Savage, J. H. King, E. W. Forster, H. J. Hodt, I. R. Jones, and D. W. Smithers. *Brit. J. Radiol.* 26: 57-72, February 1953.

The 2-mev Van de Graaff apparatus for rotation therapy which is the subject of this paper was designed and developed at the Massachusetts Institute of Technology and has been in operation at the Royal Cancer Hospital, London, for two years. Different aspects of the operation of this unit are taken up by the various authors in turn.

After an introduction by Smithers, the methods of beam definition and direction are discussed by Wheatley, Hodt, and Savage, who include also a consideration of protection problems. Since the installation is in the basement of a multistoried building, the necessity arose of protecting against upward radiations in all positions of the machine. This was met by the use of heavy alloy blocks designed to form a collar around the tube and to reduce the angle of the cone.

The engineering features of the rotating floor are described by King, Forster, and Wheatley, and problems of operation and maintenance of the unit by Jones. Dose distribution for single fields and three-dimensional dose distribution with rotation technics are discussed by Wheatley and Steed, respectively.

Smithers concludes with a brief summary of the first two years of clinical experience with the Van de Graaff generator. One hundred and nine patients had been treated, by the end of April 1952, for tumors of the bladder, bronchi, brain, uterus, and esophagus, as well as for certain other miscellaneous malignant lesions [not enumerated]. Since many of the patients had advanced disease and the time has been so short, ultimate evaluation of the results was not feasible. It was evident, however, that palliation at least can be obtained with much less discomfort to the patient than with other methods. As much as 7,000 r has been given to a volume of tissue 6 cm. in diameter at a depth of 8 to 9 cm., producing only a faint erythema and no constitutional reaction. The most satisfactory results were obtained in the advanced inoperable tumors of the bladder. Of 26 patients, 20 were alive and for the most part symptom-free, 4 for more than a year.

Twenty-seven figures. SYDNEY J. HAWLEY, M.D.
Seattle, Wash.

RADIOACTIVE ISOTOPES

Radioiodine 131 in the Diagnosis of Thyroid Function. M. W. Johns, J. H. Gregson, G. C. Foster, C. H. Jaimet, and H. G. Thode. *Canad. M. A. J.* 68: 132-137, February 1953.

The authors, from McMaster University, Hamilton, Ontario, discuss chiefly the physical and chemical measurements on which diagnosis is based in studying thyroid disorders with radioiodine. They have carried out diagnostic studies in over 500 patients and have treated and cured over 150 cases of hyperthyroidism, producing only one case of hypothyroidism.

Three separate measurements of thyroid function are made: (1) the radioiodine uptake of the gland twenty-four hours after oral administration; (2) the protein-bound radioiodine in the blood, which involves the secretion of thyroxin into the blood during the first twenty-four hours after the radioiodine is administered; (3) regional counting in patients who have nodules in the gland.

The conversion ratio (the ratio of the protein-bound I^{131} in a sample of plasma to the total I^{131} content of the same quantity of plasma) has been found to be the most reliable test for thyroid function. In cases where the conversion ratio and the radioiodine twenty-four-hour pickup were in disagreement, the conversion ratio most often gave the correct diagnosis. The conversion ratio test also gave advanced warning of a hyperthyroid condition in many cases before clinical symptoms were apparent.

In addition to the hyperthyroid cases, the authors studied 20 cases of carcinoma of the thyroid and treated 9. Five completely hopeless patients who were operated on are now, some two years after therapy, completely well.

Five illustrations; 3 tables.

JOHN M. KOHL, M.D.
Jefferson Medical College

A Simplified Technique for the Diagnosis of Hyperthyroidism, Utilizing the One-Hour Uptake of Orally Administered I^{131} . Kenneth R. Crispell, William Parson, and Philip Sprinkle. *J. Clin. Endocrinol. & Metab.* 13: 221-224, February 1953.

The thyroid uptake following oral ingestion of a tracer dose of I^{131} is widely accepted as a screening test for hyperthyroidism and hypothyroidism. The authors performed uptake determinations on 182 fasting subjects, employing a scintillation counter at 20 cm. distance, both one and twenty-four hours after 4 to 8 microcuries of I^{131} were given by mouth. One hour determinations were also made on 43 persons after 4 to 8 microcuries were administered intravenously.

Thirty-two patients with clinical diagnoses of hyperthyroidism, substantiated by a response to therapy, had one-hour uptakes ranging from 20 to 57 per cent. Ninety-six individuals clinically euthyroid had values ranging from 7 to 19 per cent. Twenty-four-hour values for the two groups were 46 to 98 per cent and 13 to 46 per cent respectively. No instance in which the one- and twenty-four-hour uptakes did not correlate in differentiating between the hyperthyroid and euthyroid state was noted.

Six persons with myxedema had one-hour uptakes from 4 to 14 per cent, compared with 7 to 19 per cent in 96 euthyroid patients. Twenty-four-hour values

ranged from 1 to 10 per cent and 13 to 46 per cent respectively. The results with one-hour determinations after intravenous and oral administration were comparable in both hyperthyroid and euthyroid groups.

The one-hour uptake after oral tracer administration may be used to screen the hyperthyroid from the euthyroid state. In differentiating between hypothyroid and euthyroid states there was considerable overlap when the one-hour uptake was used. The twenty-four-hour method remains the procedure of choice for this differentiation.

Two graphs.

R. F. LEWIS, M.D.
Cleveland Clinic

Instrumentation for Thyroid Measurement. Gordon L. Brownell and John B. Stanbury. *J. Clin. Endocrinol. & Metab.* 13: 210-220, February 1953.

The problems of measurement of I^{131} in thyroid study are placed in three categories by the authors: absolute measurements, directional counting, and body fluid analysis. The difficulties and technics of instrumentation of each are described.

Two principal sources of error are encountered in absolute measurement: the uncertainty of the source in the body and the scattering and absorption of radiation by the tissues. In most cases, accurate positioning of a single counter in relation to the gland is satisfactory. To preclude the necessity of positioning in relation to the source of radiation, Freedberg's device employing four detectors placed equidistantly on a circle about the patient's neck is used by the authors. The sensitivity and efficiency of such an arrangement are discussed at length.

Directional counting employs a single detector and a lead collimator with a suitable aperture. The counting rate is inversely proportional to the area of the aperture. The arrangement the authors use for determinations in gross regions of the body, for measuring uptakes in patients who cannot be placed in the four-tube arrangement, and for following the time of uptake by the gland, is described and illustrated.

The difficulties of body fluid analysis are discussed, and methods for urine and plasma determinations are described. The sensitivity of measurements of I^{131} in urine is approximately the same as that of *in vivo* determinations. This makes it possible to measure the urine in most instances in a flask placed directly in the four-tube array, since the correction factor for absorption and scattering is independent of wide variations in the quantity of urine. More active urine may necessitate measurement of a 100 c.c. aliquot or a few milliliters placed adjacent to one of the counters.

Eight illustrations; 1 table. R. F. LEWIS, M.D.
Cleveland Clinic

Performance of a Sodium Iodide Scintillation Counter in Measurement of I^{131} Uptake by the Thyroid. R. A. Shipley and R. E. Clark. *J. Lab. & Clin. Med.* 41: 179-187, February 1953.

Uptake of radioactive iodine by the thyroid is commonly estimated by comparison of a count obtained over the gland with the count of a standard solution of the isotope placed at the same distance from the counter. Certain precautions are necessary, however,

to insure that the count over the neck is a reasonably true measure of the actual thyroid content. Chief sources of error are radioactivity in surrounding tissues, scatter, and inaccuracies of estimation of distance to the center of radiation.

A scintillation counter is described here which meets some of these problems. The phosphor consists of a single crystal of NaI (Tl) in a sealed moisture-proof container. The high efficiency of the counter for gamma radiation makes it suitable for a wide variety of applications. For routine determination of thyroid uptake of I^{131} , it may be placed far enough from the gland to eliminate serious errors of geometry. A 1/16-inch filter of lead eliminates the appreciable augmentation of count due to back-scatter from tissue adjacent to the thyroid.

Three illustrations; 2 tables.

Analysis of Radioiodine Therapy of Metastatic Tumors of the Thyroid Gland in Man. S. H. Wollman. *J. Nat. Cancer Inst.* 13: 815-828, February 1953.

In this paper an analysis is made of the problem of radioiodine therapy of metastatic functional carcinomas of the thyroid gland in man, with a view toward determining quantitative conditions under which one might hope to destroy functional metastases with a single dose of radioiodine. It is recognized that complete destruction is an extreme goal. In slow-growing functional tumors, however, significant prolongation of active life may be achieved even though destruction is incomplete.

The author first sought to determine the minimum level of functional activity of a tumor at which I^{131} concentration would be sufficient to produce destruction. It is assumed, at the outset, that the maximum single dose of I^{131} that can be safely given is 100 to 250 mc. The 100 mc. figure was chosen as a lower limit because it is in wide use and appears safe, although it gives total-body irradiation of approximately 100 r and occasionally twice this. The 250 mc. figure is the highest reported to be in general use, although occasionally a single dose of over 300 mc. has been used with minimal side effects. The limiting factor in dosage is the incidental total-body irradiation before the I^{131} is cleared from the blood by the thyroid gland, tumors, and kidneys, and again after its removal from the blood, since it returns in bound form. In general, the tissues limiting radioiodide dosage in man are the blood-forming ones.

It is further assumed that radiosensitivity of a tumor is independent of its mass and that the minimum amount of I^{131} which must be concentrated in a tumor to destroy it is 100 to 300 μ c. per gram. Finally, the standard value for concentration of I^{131} by the thyroid gland is taken as 1.75 per cent of the administered I^{131} per gram of thyroid tissue. This figure is calculated from an uptake of 35 per cent of the dose of I^{131} by a thyroid gland whose average weight is 20 gm. Using these figures, it is possible to estimate the ratio of the concentrations of I^{131} in thyroid and non-thyroid tissues in a standard 70-kilo man. This concentration ratio would imply that for such a dose of I^{131} , 12,000 r to the thyroid would yield only 1 r total-body irradiation, which is many times too low.

It was found that the required I^{131} uptake per gram of tumor for complete destruction varied from 1/6 (for an assumed concentration of 100 μ c. per gram) to 1/44 (for 300 μ c.) that of the thyroid gland of a standard

man. The size of the tumor plays a significant role. The upper limit of permissible tumor weight can be calculated by assuming all the administered I^{131} to be collected by the tumor. However, as the tumor mass decreases, if any dimension becomes smaller than the average range of the I^{131} beta particles, there will be a delivery of I^{131} to the tumor greater than the specified 100 to 300 μ c. per gram. Then a significant fraction of the beta radiation from the accumulated I^{131} will be lost without being absorbed by the tumor, thus reducing the destructive action.

Estimates may be made of the dose of radiation at the center and surface of a spherical tumor in which the range of the I^{131} beta rays is larger than the radius of the tumor. Dosages at the surface of the sphere are less than those at the center at all diameters. Consequently, a small tumor requires for its destruction an I^{131} concentration higher than that assumed previously. In view of this, a metastatic colony consisting of only a few cells could not be destroyed even if its functional activity were significantly greater than that of normal thyroid tissue. This effect is a serious limitation on isotope therapy of metastatic tumors in general. The most obvious method of overcoming the loss of radiation from small metastases is to use isotopes with radiation of short range, such as alpha particle emitters.

Relatively few data are available on the functional activity of tumors of the thyroid gland, but it appears that in only a few cases could destruction of the tumor be expected with a single dose of I^{131} .

Two factors causing major difficulties in controlling I^{131} uptake are: (a) the variation in histologic and biochemical properties from tumor to tumor and within a single tumor, and (b) inability to determine tumor weights or the total weight of each different type of tumor tissue present. These factors were studied in mice bearing transplantable thyroid tumors, and it was found that different strains of tumors have different rates of clearance, with a constant ratio in the same individual of I^{131} content in tumor and thyroid gland, but this ceases to be true when organic bound I^{131} begins to be secreted by the thyroid or tumor. This is a problem needing more investigation. It was also found in mice that the maximum tumor uptake is proportional to tumor weight for all lines, provided the uptake is not too high.

In an animal in which the thyroid gland, kidney, and tumor compete with each other for administered I^{131} , the isotope is expected to be divided among the three competing tissues in proportion to their clearance, but this does not hold invariably. The relation between tumor uptake and clearance follows a characteristic "saturation curve," and the "saturation effect" begins where uptake and clearance deviate from proportionality.

The author does not feel that administration of a series of test doses until retention by the patient or tumor is at a maximum, followed by a therapeutic dose, is advisable. If increases in uptake by a tumor are due to increases in the mass of functional tissue rather than to increases in uptake per gram of tumor, there is no advantage in delaying the therapeutic dose, and there may actually be a disadvantage. This is so especially if, because of growth, tumor uptake becomes great enough for saturation to occur. In this case, uptake per gram will no longer be maximal because of the saturation effects.

JOHN F. BERRY, M.D.
Louisville General Hospital

Radioiodine Uptake by Transplantable Tumors of the Thyroid Gland in C3H Mice. I. Experimental Results. S. H. Wollman, R. O. Scow, B. Wagner, and H. P. Morris. *J. Nat. Cancer Inst.* **13**: 785-805, February 1953.

Radioiodine Uptake by Transplantable Tumors of the Thyroid Gland in C3H Mice. II. Theory. S. H. Wollman. *Ibid.*, pp. 807-814.

The experimental study reported in the first of the papers listed above was carried out on C3H mice bearing transplantable thyroid tumors, implanted in subcutaneous or intramuscular sites. The uptake of I^{131} by the thyroid gland and the tumors was determined at various time intervals after injection of the isotope.

Some tumors of the more active type were found to have a total uptake many times greater than the thyroid gland, and this was accompanied by a decrease in the uptake by the gland. When uptake by either the thyroid or the tumor was large, then uptake by the corresponding tumor or thyroid was decreased. The I^{131} uptake by the tumor was proportional to the tumor weight when the uptake was less than 25 per cent of the administered dose; tumor uptake increased less rapidly than the weight when the uptake was higher.

The uptake per milligram of thyroid gland divided by uptake per milligram of tumor for the more active tumors was a constant, independent of the time after I^{131} was administered for the intervals studied (two to forty-nine hours). It was thus possible to classify the tumors on the basis of the ratio of their uptake per milligram to that of the thyroid of the host. On this basis, tumor activity was found to range from 1/10 to less than 1/600 of that of the thyroid.

No definite stimulation of functional activity by Thiouracil feeding was observed in two independent tumor lines of low functional activity.

Analyzing the accumulation of I^{131} by normal thyroid tissue, kidney, and functional transplanted tumors in the mice of the series reported above, Wollman developed a theory "which predicts, in qualitative agreement with experimental studies, the following: (1) the condition for competition between thyroid gland and tumor; (2) the linear increase of tumor uptake with tumor mass for small uptakes; (3) the relative independence of tumor uptake and tumor mass for large uptakes; (4) the constant ratio of tumor uptake per mg. to thyroid uptake per mg. independent of time after I^{131} administration."

It is also shown how to indicate, on the basis of these observations, the extent of increase in organ uptake due to kinetic effects when a competing organ is removed.

The experimental report is illustrated by 4 photomicrographs, 17 graphs, and a table.

THOMAS E. PADGETT, M.D.
Louisville General Hospital

Rate of Uptake of Fluid from Lung Measured with Radioisotopes; Comparison of Rapid Rate for Water with Slower Rate for Saline. Gene Qualls, Howard J. Curtis, and George R. Meneely. *Am. J. Physiol.* **172**: 221-225, January 1953.

Radioactive iodine (I^{131}) in the form of NaI and sodium 24 in the form of NaCl are convenient labels for estimating uptake by the body of fluid introduced by tracheal catheter into the lungs of dogs. In 37 experiments normal saline (0.9 per cent NaCl) solution

introduced into the lung in volumes of 1.0 to 6.0 ml./kg. body weight disappeared with a half-time of 15.5 ± 0.8 minute (S.D. 4.4); in 13 experiments distilled water similarly introduced disappeared with a half-time of 3.8 ± 0.4 minute (S.D. 1.4). These mean half-times differ by a factor of four. In the present investigation a marked variability was found in the half-time from dog to dog and in the same dog on different days. This did not vary in any consistent manner with state of hydration, venous pressure, respiration rate, liquid or atomized administration, hematocrit value, or plasma protein level. When repeated determinations of uptake either of water or of saline were made on the same day, quite reproducible half-times were obtained. This would indicate that determination of the half-time for uptake of water or saline constitutes a measure of the osmotic-oncotic pressure gradients between alveolus and capillary which exist as of the moment.

One drawing; 3 graphs.

Radioactive Phosphorus (P^{32}) in Treatment of Menorrhagia. H. C. McLaren, J. C. Heath, and A. Quinton. *Brit. M. J.* **1**: 358-363, Feb. 14, 1953.

If menorrhagia persists after curettage in patients over forty, a decision on radical treatment either by induction of the menopause or by surgery may be necessary to avoid anemia and increasing general debility. The authors' procedure of irradiating the uterus with beta particles and thereby destroying the endometrium is not a new idea. One difficulty in the past has been the construction of an applicator which would pass the human cervix yet allow irradiation of the whole cavity of the uterus.

For the experiments described in this paper, first in animals and later in patients, a simple acrylic rod or a cylindrical "perspex" former was used, around which was molded filter paper whose surface was covered with a solution of P^{32} . This was allowed to dry and was covered, in turn, by a coating of acrylic resin or "perspex."

The P^{32} produced a surface burn of the endometrium 2 mm. in depth, without ovarian damage. The reaction healed in ninety days, with endometrial regeneration. Menstruation usually reappeared, and of 11 patients subjected to a three-month trial, 7 were cured of menorrhagia and two improved. Two cases, in which unsuspected fibroids were present, were failures.

The carcinogenic action of x-rays or repeated small doses of gamma rays on the skin raises the possibility of endometrial cancer as a sequel of beta irradiation of the uterus. It is felt that, if the endometrium heals and normal menstruation ensues, it is unlikely that cancer will develop, but prolonged follow-up is of course necessary. The possibility of fetal abnormality is discussed as a theoretical objection to this treatment.

Experiments are now in progress with cerium (Ce^{141}), which should produce a deeper endometrial burn, which in turn should give better clinical results.

Four photomicrographs; 3 tables.

L. R. JAMES, M.D.
Boston, Mass.

Thorium-X in Dermatology. John van de Erve, Jr. *South. M. J.* **46**: 155-160, February 1953.

Thorium-X is a natural radioactive isotope of radium which emits alpha rays. It has a half life of 3.65 days. Alpha particles may be stopped by a thin sheet of

cardboard, but studies by Lomholt showed diffusion into tissues of 70 microns depth, while Witten *et al.* have demonstrated activity in sweat glands as deep as 1.8 mm. below the surface. This penetration is largely down the follicles and sweat ducts and is not diffused through the tissue. Practically all activity is concentrated in the first 80 microns or 0.08 mm. depth, and scattered radiation deeper has little biological effect.

The material used in the study reported here was made up into alcohol solution containing 150 microcuries per cubic centimeter and was diluted with one to three parts of isopropyl alcohol for working solutions when used widely over the body, as in extensive psoriasis. The ointment form was used in a strength of 75 microcuries per gram and was applied for twenty-four-hour periods. For mucous membranes and inflamed areas the time was much shorter. At the end of the prescribed periods, the patient was instructed to remove the application. Patients were not allowed to make their own applications.

The results obtained in 225 cases of various dermatological conditions are tabulated. These cases were among some 250 seen during a five-year period. The author had no apparent results in several cases of alopecia areata. In angiomas (not including the cavernous type), Thorium-X was found to be an excellent agent for "trimming" the islands and edges left over after deeper therapy with radium and x-rays. It yielded much superior results to carbon dioxide snow and produced less scarring. It was felt to afford a good superficial method of therapy for the very thin keratoses and for herpes and superficial inflammatory changes and leukoplakia. In these conditions, however, the treatment may be dangerous and one must not overtreat.

In general, fungous infections of the feet, hands, and glabrous skin of the body, and paronychia (other than monilia), responded to Thorium-X in the same manner as they do to moderate roentgen irradiation but other methods of therapy are felt to be more important. Six cases of herpes simplex were treated and in these it was felt that Thorium-X offered certain advantages over x-rays. For keratosis senilis an average of three applications at two-week intervals of 150 microcuries resulted in disappearance of most of the lesions without further trouble. Lichen planus, lichen simplex chronicus, lichen simplex nuchae, lymphangioma circumscriptum, pruritus ani, vulvae and scroti, psoriasis, and verruca acuminata were all helped in varying degrees. Attention is called to some of the adverse reactions, such as persistent pigmentation and hyperkeratosis, following prolonged exposure.

Four illustrations; 1 table.

JOHN M. KOHL, M.D.
Jefferson Medical College

Studies on the Renal Excretion of Radioactive Digitoxin in Human Subjects with Cardiac Failure. G. T. Okita, F. E. Kelsey, P. J. Talso, L. B. Smith, and E. M. K. Geiling. *Circulation* 7: 161-168, February 1953.

The authors studied the renal excretion of digitoxin labeled with carbon 14 in 3 cardiac patients. The method and results of the investigations are described. Use of the tracer technic permits not only the detection of minute amounts of the labeled drug (0.02 microgram), but one is able to follow the metabolic products of the parent compound.

Approximately 60 to 80 per cent of an administered dose is eliminated through the kidneys, suggesting that this is the major route of excretion of digitoxin in cardiac patients. There is a marked initial excretion of the drug during the first two days, followed by a gradual leveling off of the excretion gradient. Minute amounts of unchanged digitoxin have been detected in the urine up to the fortieth day after administration of a single dose, while C¹⁴-labeled compounds were detected up to the seventy-fourth day. Only 6 to 10 per cent of the original drug is excreted as "unchanged" digitoxin; the remainder is eliminated as metabolic products.

Five figures; 2 tables.

SEYMOUR A. KAUFMAN, M.D.
Boston, Mass.

Transbronchial Instillation of Radioactive Gold Colloid in the Lung of the Dog. Distribution Studies, Survival and Pathology. George R. Meneely, Stewart H. Auerbach, Clarence C. Woodcock, Ross C. Kory, and Paul F. Hahn. *Am. J. M. Sc.* 225: 172-177, February 1953.

Experiments on dogs were designed to localize a radioisotope in the lung and the regional lymph nodes through exploitation of the physiology of pulmonary lymphatics in relation to colloidal material. Distribution studies following introduction of radioactive gold colloid (particle diameter approximately 0.05 micron) into the pulmonary alveoli of 6 dogs *via* the tracheobronchial route showed that (1) the colloid is fixed early in the ipsilateral lung and does not spread to the contralateral side of the chest, (2) significant amounts of the colloid reach the mediastinal nodes by the second week, and (3) the colloid does not enter the blood stream in any consequential amount. Survival after doses of 1 mc. or more per kg. is poor. Doses of 0.66 mc. and 0.50 mc. per kg. are fairly well tolerated.

In dogs sacrificed twenty-four hours after a dose of approximately 5,000 r, there were a mild acute non-necrotizing pneumonitis, intra-alveolar edema, and mild polymorphonuclear infiltration in the ipsilateral lung. The most affected lobe showed acute edema of the pleura and the subpleural interstices. In the contralateral lung patches of atelectasis alternated with acute emphysema. After four days, the disease process consisted mainly of areas of alternating atelectasis and acute emphysema. After six days, small areas of partial collapse were present with slight emphysema in the areas of high dosage.

Lymph nodes at twenty-four hours exhibited little radioactivity but showed dilated sinusoids containing numbers of polymorphonuclear cells and erythrocytes. Erythrophagocytosis by the large mononuclear cells was pronounced. Small areas of cortical necrosis were found in nodes having higher radioactivity. After four days the nodes showed loss of well defined follicles and loss of lymphocytes from areas of the cortex. There was a relative increase in the reticulum cells, but few mitoses were found. After six days the most active nodes were devoid of follicles. Cortical reticulum cells were increased at the expense of the lymphocytes. The cortices were depleted of normal cells, but there were moderate numbers of mitotic figures among the reticulum cells. After fifteen days the changes were more advanced, but there was also evidence of regeneration in the form of pale hyperplastic follicles capped with crescents of lymphocytes.

In animals receiving from 0.5 to 1.0 mc. of radioactive gold per kg. in the intermediate lobe of the right lung, the local pathological process was much more severe than that described above, where the dose was more diffusely distributed. The principal local lesion was an area of necrosis with central softening or abscess cavity.

These studies indicate that this method of introduction of colloidal gold is unsatisfactory for cancer therapy, since the lung, where the isotope lodges, is too heavily irradiated, and the regional lymph nodes receive only trivial amounts of radiation because the activity of the gold is largely spent before it reaches them.

Two tables.

RICHARD F. McCLURE, M.D.
Palos Verdes Estates, Calif.

Distribution of Administered Radioactive Rubidium (Rb^{86}) in Normal and Neoplastic Tissues of Mice and Humans. Albert Zipser and A. Stone Freedberg. *Cancer Research* 12: 867-870, December 1952.

Rubidium is an alkali metal in the same series of the periodic table as lithium, sodium, cesium, and potassium, and has chemical and physical properties particularly similar to potassium. The isotope, Rb^{86} , used in the present study, has a half-life of 19.5 days and emits both beta and gamma rays. Preliminary studies showed a relatively small uptake of Rb^{86} by normal brain tissue after parenteral administration of Rb^{86} carbonate in the guinea-pig and dog.

Six Swiss white mice bearing sarcoma 37, transplanted three weeks earlier, and an equal number of control animals were given intraperitoneal injections of a solution of Rb^{86} , providing approximately 8.2×10^6 counts per minute. The animals were sacrificed twenty-four hours after the administration of the isotope. The sarcoma was found to concentrate less rubidium than the brain. In a further experiment it was found that the greatest uptake by the tumor occurred during the first sixteen days following its transplantation.

Eight ABC strain mice with subcutaneously implanted neuroblastomas and 8 C3H strain mice bearing astrocytomas, transplanted three weeks and six weeks earlier, were used in another part of the study. One-half of the mice were given Cs^{134} in the form of cesium chloride and the remainder were given Rb^{86} . In each group of animals the absolute uptake of both isotopes by tumor and brain tissues was greater at twenty-four hours than at four hours. In every instance, however, the ratio of the Rb^{86} concentration in the tumor to that in the brain was greater at the four-hour interval.

A man who was to undergo craniotomy for an intracranial neoplasm was given an intravenous injection of a 13 per cent solution of Rb_2CO_3 , containing 100 μ c. of Rb^{86} , fifty minutes before the operation. Biopsy specimens obtained during the operation and specimens of other tissues obtained at autopsy were analyzed for Rb^{86} content. A second patient being operated upon for further resection of a glioblastoma was given an intravenous injection of a solution of Rb_2CO_3 containing 100 μ c. of Rb^{86} after the surgical procedure was under way. Specimens of the glioblastoma and of normal brain were secured at random intervals until the operation was completed.

The brain tumors both in the mice and in the human beings were found to have taken up from 6 to 19.3

times more Rb^{86} per gram than did normal brain tissue. These ratios of concentration are sufficiently great to warrant the use of this isotope in attempted localization of intracranial neoplasms by means of external counting devices.

The pancreas demonstrated the highest concentration of administered Rb^{86} , followed closely by liver and spleen. The absolute majority of the isotope is distributed to the entire skeletal muscle of the body.

Toxicity studies in mice showed that rubidium has a profound effect upon musculature. Overdosage produced generalized spastic paralysis leading to respiratory failure. The MLD 50 for mice is 0.65 mg. Rb_2CO_3 per gram of body weight. Doses of Rb^{86} adequate for localization studies in man are well below the range of toxicity.

Five tables.

Intracellular Distribution of Radioactivity in Nucleic Acid Nucleotides and Proteins Following Simultaneous Administration of P^{32} and Glycine-2- C^{14} . Evelyn Pease Tyner, Charles Heidelberger, and G. A. LePage. *Cancer Research* 13: 186-203, February 1953.

Glycine-2- C^{14} and P^{32} were simultaneously injected intraperitoneally into normal rats and others bearing multiple Flexner-Jobling carcinoma transplants. The animals were sacrificed after various time intervals, and the livers and tumors were fractionated by differential centrifugation into nuclear, mitochondrial, microsomal, and supernatant fractions. From each fraction the nucleic acids were isolated, hydrolyzed, and the nucleotides were separated by ion-exchange chromatography. The specific activity of the nucleotides with respect to P^{32} was determined, the purine nucleotides were hydrolyzed, and the C^{14} specific activity of the purines was measured.

From the data on the acid-soluble phosphorus and uncombined glycine, it was concluded that the metabolic pool sizes of these are similar.

At early time intervals the order of decreasing specific activity of both isotopes in the RNA (ribonucleic acid) cell fractions was nuclei, supernatant fraction, microsomes, and mitochondria.

At early times the C^{14} specific activity of the proteins was highest in the microsomal fraction. The relationship of this finding to those for the RNA is discussed.

The specific activity of the DNA (deoxyribonucleic acid) and RNA nucleotides in tumors was higher at all times than in the corresponding liver nucleotides.

The specific activities of the P^{32} and C^{14} in the purine nucleotides from DNA were similar, indicating that both precursors are incorporated into some intermediate at the same time.

The specific activity of the P^{32} in the RNA purine nucleotides of normal liver was considerably higher than that of the C^{14} . This indicates that the phosphorus is incorporated into an intermediate at an earlier time than is the glycine.

The total radioactivities in the RNA nucleotides of all cell fractions are directly proportional to the total quantity of the nucleotides present. This suggests that the composition of the nucleic acid determines the amount of synthesis and, further, that the RNA molecule is synthesized as a whole from the component nucleotide precursors.

The nucleic acid metabolism of tumors appears to be qualitatively similar, but quantitatively more rapid than that of liver.

The systemic effect of a tumor on the metabolism of liver is manifested in an increased specific and total radioactivity of the DNA nucleotides in the livers of tumor-bearing animals as compared to those of normal liver.

A tentative scheme of nucleic acid biosynthesis with respect to adenylic acid has been proposed in order to account for these findings. The significance of this tentative scheme is discussed.

Eighteen charts.

Laboratory Factors Influencing the Determination of Plasma Volume Using Human Albumin Tagged With I^{131} . Stanley Levey, Jean Hower, and Ruth H. Loughridge. *J. Lab. & Clin. Med.* 41: 316-322, February 1953.

Serum albumin tagged with radioactive iodine offers a good tool for the determination of plasma volume, since the albumin mixes well with the blood and leaves the vascular tree slowly; the isotope is easily detected with a Geiger-Müller or scintillation counter; small amounts of hemolysis do not interfere in the deter-

mination of the radioactivity; and the amount of radioactive material used is too small to produce any untoward effect.

The authors consider here certain technical factors involved in making plasma volume determinations by this technic. The counting dishes must have perfectly flat bottom. After the plasma is pipetted into them, the dishes must be allowed to dry on a level surface. If these precautions are not observed, one may obtain dried films of protein possessing different thicknesses in different areas. The unevenness of the film can cause large discrepancies in the counts recorded. Providing one obtains uniformly dried layers of protein in the counting dishes, it is possible to count the sample as close to the Geiger-Müller tube as practical. The moving of the sample carrier closer to the tube will allow a much more rapid count without increasing the variation of the procedure. The glassware used in carrying out a determination with human plasma tagged with I^{131} can be washed in any of the usual manners employed in the chemical laboratory to render it free of radioactive contamination.

RADIATION EFFECTS

Lethal and Tolerance Doses of X and Gamma Rays in Man During General Irradiation. F. Běhouněk and M. Majerová. *Acta radiol. et cancerol. bohemoslov.* 7: 5-18, 1953. (In Czechoslovakian, with English summary)

A comparison is made of whole-body irradiation by the gamma rays produced by explosion of an atomic bomb and clinical experience with spray irradiation as reported by different authorities. It appears that man can tolerate a whole-body dose of as much as 480 r to the skin without lasting effect if it is suitably fractionated and a single dose does not exceed 30 r.

The surface doses were converted into integral doses (Mayneord and Clarkson: *Brit. J. Radiol.* 17: 177, 1944; Mayneord: *Ibid.* 359), and it was found that the latter for various sources of x-rays and gamma rays varied but little if the energy of the radiation lay between 0.1 and 3.0 mev. Stress is laid on the considerable difference in integral dose received by workers with diagnostic x-rays and those with deep x-rays or gamma ray sources at an equal tolerance surface (skin) dose of 0.5 r per week. Workers in the latter category receive during their lifetime a dose twice as high as the median spray dose (total), i.e., doses of such an order as would in a single application have a devastating medical effect. The substantially different biological reaction is the clearest evidence of the basic biological significance of the temporal distribution of ionization, brought about by the absorption of x-rays and gamma rays in the organism.

Three illustrations.

Comparison of the Effect of Roentgen and Radium Radiation on the Human Skin. F. Wachsmann, with the assistance of G. Barth, H. Fetzer, J. Ries, and G. Schulte. *Strahlentherapie* 90: 438-445, 1953. (In German)

Erythema studies were made on 40 elderly cancer patients and on the skin of pigs. Roentgen radiation from 45 to 200 kv. was used and radium sources of 400 and 1,200 mg. A tissue-equivalent filter was added to compensate for the increase in percentage depth dose

with ultra-hard rays. Gamma radiation was given at a distance of 10 mm. with 1-mm. brass and 3-mm. Al filters. The field sizes, percentage depth dose, and dose rates were identical.

The experiments showed that, with the same technical factors, it takes three times as many roentgens of gamma rays as of x-rays to produce a threshold erythema; to produce an epitheliolysis or necrosis, only two to one and a half times more gamma radiation has to be applied.

This difference in the biological effect of the radiation of roentgen rays and radium is explained by the difference in the specific ionization density, which becomes less in the harder rays. The author emphasizes that Holthusen's statement, "the biological effect of the radiation is independent of the wave length," still holds true.

Nine graphs. EUGENE F. LUTTERBECK, M.D.
Chicago, Ill.

Value of the Blood Picture for the Indication of Radiation Damage. Hanns Langendorff. *Strahlentherapie* 90: 408-420, 1953. (In German)

This is a report on the effects of total-body irradiation of 30 white male rats receiving 2.5 r daily for a year (92 kv., 10 ma., 0.5-mm. Al filter, 80 cm. distance). Ten animals were used as controls. There was a slight decrease in the leukocyte and lymphocyte counts in both the irradiated and unirradiated animals. Histologic examination of the testes revealed a slight inhibition of spermiogenesis. The spleen showed a mild degree of reduction of lymphatic tissue and loss of some of the cell-forming centers. The follicles remained unchanged.

These results confirm those of others, as Lawrence, Dowdy, and Valentine (*Radiology* 51: 400, 1948) and Jacobson, Marks, and Lorenz (*Radiology* 52: 371, 1949), who found a minimum daily dose of 4.4 r necessary to cause a decrease in the number of leukocytes and lymphocytes and 8.8 r to cause a reduction in red cells.

The author concludes that the blood picture is value-

less in determining damage due to small amounts of radiation received over a long period of time.

Nine photomicrographs; 2 graphs.

EUGENE F. LUTTERBECK, M.D.
Chicago, Ill.

Comparison of Local and System Exposures in Production of Radiation Cataract. A. C. Upton, K. W. Christenberry, and J. Furth. With the technical assistance of J. R. Thomson. *Arch. Ophthalmol.* 49: 164-167, February 1953.

It is well known that cataract may result from exposure to ionizing radiations, but the pathogenesis of the lesion is not fully understood. Since opacification of the lens is also produced by a variety of chemical, metabolic, and endocrine disorders, the biochemical disturbances resulting from whole-body irradiation might be expected to contribute to cataractogenic effects. Were the lens injured indirectly in this way the threshold cataract-inducing dose of radiation would depend in part upon the degree of general body damage or upon the total volume of tissue irradiated. Likewise, some measure of protection against cataract formation might be afforded by shielding a part of the body or an organ, such as the spleen, which protects against other types of irradiation injury. The authors undertook to investigate these possibilities.

Female Rf mice seven to nine weeks of age were given 15 to 405 r of x-radiation, with the following factors: 250 kv.p., 76 to 84 r per minute, 30 ma., 3-mm. Al filtration, 37.9 cm. skin-target distance. The whole body, the head, or the body only was exposed, and the eyes of the animals were studied periodically thereafter with the slit lamp for cataract.

Opacities of the lens were readily induced in the animals receiving irradiation of the whole body or the head, the threshold dose being somewhat less than 15 r. The opacities increased in severity with the dose and time after irradiation, the incidence of lesions approaching 100 per cent at thirty-three weeks after exposure to doses of 45 r or more. Cataract induction appeared to depend upon exposure of the eye itself, since no cataractogenic effects were detected after exposure of the remainder of the body to a wide range of doses. It is probable, from evidence now available, that cataract results from radiation injury of the cells of the anterior epithelium of the lens.

It is significant that the sensitivity of the lens to cataract induction is not increased with whole-body irradiation; in this respect the process differs from radiation injuries in general, such as damage to hemopoietic organs, epilation, and inhibition of antibody production. It is also clear from this study that appreciable protection against cataract formation is not conferred by shielding the extraocular tissues from radiation. The existence of other mechanisms of protection is indicated by the protective effects conferred upon the lens by cysteine (von Sallmann: *Arch. Ophthalmol.* 47: 305, 1952. *Abst. in Radiology* 60: 162, 1953); however, an agent of practical value in preventing radiation-induced cataract is yet to be found.

One graph; 1 table.

Histochemical Changes in Irradiated Ovaries. I. Succinic Dehydrogenase Activity. Alvan C. Foraker, Sam W. Denham, and M. Harlan Johnston. *Arch. Pathol.* 55: 147-153, February 1953.

Twelve virgin female rabbits ranging from six to

eight weeks in age and from 1,180 to 3,140 gm. in weight were each irradiated with 400 r (in air) in a single dose to a 6.0-cm. external port over the left ovary. Physical factors were: constant potential 200 kv., 18 ma., half-value layer 1.2 mm. Cu, distance 50 cm., rate 50 r per minute. Four weeks later 6 of the rabbits were given intravenous injections of urine from non-pregnant women, and 6 of urine from pregnant women, according to a standard routine for the Friedman test, except that the second injection was given after a twenty-four hour interval. Forty-eight hours after the first injection, the non-irradiated ovaries of all animals presented the classical appearance of either a negative or positive test. In contrast, the irradiated ovaries were smaller, paler, and firmer. Tissue from all ovaries was incubated in neotetrazolium with succinate to demonstrate succinic dehydrogenase activity.

Little evidence was found of irradiation damage to stromal cells, either in general pattern or in succinic dehydrogenase activity, as manifested by formazan deposition in irradiated and non-irradiated ovaries.

Most of the ova in the irradiated ovaries were obliterated. Those remaining were largely atretic, with little follicle-cell formation.

There was little evidence of ability of the irradiated ovaries to respond to the hormonal stimulation of the Friedman test.

Eight photomicrographs.

Effect of X-Irradiation on Fat Balance and on Lipid and Vitamin A Content of the Liver. John G. Coniglio, William J. Darby, Mary Catlett Wilkerson, Richard Stewart, Anne Stockell, and Granville W. Hudson. *Am. J. Physiol.* 172: 86-92, January 1953.

Fat absorption in irradiated rats was studied over a 28-day period by use of the balance method. A total of 500 or 650 r (including back-scatter) total-body irradiation was delivered, at 200 kv., 20 ma., with 0.5 mm. Cu and 1.0 mm. Al filtration. Rice was used as backing to obtain uniform back-scattering.

No significant difference was observed between irradiated and pair-fed control animals in the amount of fat excreted during the post-irradiation period as the percentage of ingested fat lost in the stools. In both irradiated and control rats fat excretion was decreased in the post-irradiation period, a result probably of decreased food intake. Studies of liver lipids in irradiated and pair-fed control animals at intervals from two to forty-two days after irradiation revealed no significant change in total lipids, phospholipid, or total cholesterol directly attributable to the irradiation. No significant changes were observed in liver vitamin-A concentrations due to irradiation.

The authors emphasize the importance of paired feeding in studies of metabolic effects of irradiation.

Two graphs; 4 tables.

Effect of Exposure to Cold on Response of the Rat to Whole Body Radiation. J. C. Barlow and E. A. Sellers. *Am. J. Physiol.* 172: 147-151, January 1953.

Many of the changes noted after whole-body irradiation are similar to those found following other stresses and thus may be considered to be of a non-specific nature. It occurred to the authors that the changes involved in acclimatization to cold, which is considered representative of any "non-specific" stress, might modify an animal's ability to resist sublethal and lethal doses of whole-body irradiation. The possible cumula-

tive effect of a dual stress (radiation and cold) on survival also seemed worthy of investigation. The experiments described deal with the response of both cold-acclimatized and non-cold-acclimatized rats which were irradiated and subsequently placed in either a cold (2°C.) or normal ($22^{\circ} \pm 2^{\circ}$) environment. The radiation factors were 200 kv., 19 ma., 1-mm. Al and 0.5-mm. Cu filtration; rate approximately 30 r per minute in air; distance 50 cm.

It was found that acclimatization to cold did not decrease the resistance of Wistar rats to whole-body radiation. When rats of equal weight were irradiated, acclimatization to cold increased survivals, but when the influence of cold on the age-weight relationship was taken into account, neither a beneficial nor an adverse effect upon survival was observed. Exposure to cold after irradiation increased the mortality rate.

Five graphs; 1 table.

Heterotransplantation of Human Cancer. I. Irradiated Rats. Sheldon C. Sommers, Rosanna N. Chute, and Shields Warren. *Cancer Research* 12: 909-911, December 1952.

Heterotransplantation of Human Cancer. II. Hamster Cheek Pouch. Rosanna N. Chute, Sheldon C. Sommers, and Shields Warren. *Ibid.*, pp. 912-914.

Heterotransplantation of Human Cancer. III. Chorioallantoic Membranes of Embryonated Eggs. Sheldon C. Sommers, Barbara A. Sullivan, and Shields Warren. *Ibid.*, pp. 915-917.

In the first of three studies the authors used a method described by Toolan (*Proc. Soc. Exper. Biol. & Med.* 77: 572, 1951) for the transplantation of human neoplasms subcutaneously into rats previously given total-body irradiation (three doses of 200 r on alternate days). Forty of 75 cancers (53 per cent) of various types survived transplantation into the irradiated animals, though little evidence was found for growth of the transplants. They could be said to persist rather than to grow. Five of 10 second-generation implants, however, actually grew, and proliferative enlargements were identified microscopically.

A second study was carried out with hamsters. Of 65 human neoplasms transplanted into the cheek pouch in these animals, 30 (46 per cent) showed successful growth. Eleven of 20 second-generation transplants and 3 of 6 third-generation transplants were also successful. Irradiation of the host prior to transplantation had no apparent effect on survival of the tumor. Fifty-eight per cent of 12 tumors were successfully grown in both irradiated animals and in unirradiated controls.

In the third of this series of studies, transplantation was done into the chorioallantoic membranes of chicken

egg embryos. Twenty-eight of 59 different human cancers (47 per cent) survived such transplantation. A total of 620 incubated eggs were used. In terms of the 327 eggs whose embryos survived transplantation, the positive yield was 23 per cent, with or without prior irradiation. The best results were obtained with sarcomas.

Six tables.

The Combined Effects of Cortisone and Roentgen Radiation upon Natural and Induced Resistance to Homoio-transplantation of Mouse Leukemia, Line I_b. A. A. Werder, Jack Friedman, E. C. MacDowell, and J. T. Syvertson. *Cancer Research* 13: 158-164, February 1953.

Investigations carried out by the authors revealed that two extrinsic agents, cortisone and ionizing radiation, convert the naturally resistant status conferred by the genetic constitution of certain inbred mice into a state of susceptibility. Mice representative of three resistant inbred strains, BALB, A, and STOL, and of the stock Swiss albino CFW strain, were made susceptible by the administration of cortisone and x-radiation singly and in combination, to the homoio-transplantation of lymphoid leukemia, Line I_b, when tested within twenty-four hours. (This line of leukemia originated spontaneously in an inbred strain of mice designated as C58. The subscript b indicates freedom from a virus which contaminated the line for a period of years.) The cortisone and irradiation operate synergistically to potentiate the alternative effect that may result from the employment of either agent singly. Contrariwise, mice made resistant by actively induced immunization with leukemic cells were little affected by the administration of the two agents singly or in combination.

Two charts; 5 tables.

Effect of Roentgen Rays on *Microsporum audouini*. An in Vitro Study. Kurt Loewenthal. *Arch. Dermat. & Syph.* 67: 191-193, February 1953.

Two freshly isolated strains of *Microsporum audouini*, growing on dextrose-peptone agar, were given one exposure each of 340 r of unfiltered roentgen rays (85 kv.; 5 ma.; 25 cm. distance; 3 minutes 25 seconds). Neither the irradiated colonies nor their descendants showed gross or microscopic changes attributable to the irradiation. In experiments previously described (*Arch. Dermat. & Syph.* 63: 750, 1951. *Abst. in Radiology* 58: 636, 1952), *Microsporum canis* under similar controlled conditions revealed acceleration and intensification of pleomorphism and degradation of the fuseaux formation. The author believes that further investigation of this apparent difference in sensitivity to a given dose of roentgen rays is necessary

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